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IN MEMORIAM

WILLIAM T. BLACK
1875-1938

WILLIAM T. BLACK, a member of the Advisory Editorial Board of the JOURNAL, was born January 12, 1875, at Stanton, Tennessee, and died December 10, 1938, at Memphis. While in the midst of an operation, he was seized with a heart attack and died within the hour. A wide circle of personal and professional friends were shocked and saddened by his sudden passing and he will long be remembered by his associates and many friends.

For a number of years he had been connected with the University of Tennessee. He received his medical education at the Memphis Hospital Medical College, which later was absorbed by the University Medical School. Later he became a valued member of the faculty and for the past four years had held the chair of Gynecology. He served faithfully and fruitfully the university of the state in which he was born and educated.

He was well known in his profession far beyond the borders of his own State, and his articles on medical subjects were published in many periodicals and recognized as important contributions in the field of gynecology.

He was a member of many national associations: The American College of Surgeons; The American Association of Obstetricians and Gynecologists; The Southern Surgical Association; The American Board of Obstetrics and Gynecology; and The Central Association of Obstetricians and Gynecologists, of which he had been vice-president. In many of these he held offices and chairmanships and these duties he always performed exceedingly well.

Dr. Black was ex-president and visiting Gynecologist at the Baptist Hospital, Consulting Gynecologist to St. Joseph Hospital, Professor of Gynecology of University of Tennessee, Visiting Gynecologist to John Gaston Hospital, and Visiting Gynecologist to the Shelby County Almshouse.

His charm of personality, his sterling qualities of character and his deep and abiding interest in humanity and his profession endeared him to all. He will be grievously missed by all who were associated with him.

W. T. PRIDE, M.D.

Original Communications

THE OCCURRENCE AND SIGNIFICANCE OF NUCLEATED ERYTHROCYTES IN THE FETAL VESSELS OF THE PLACENTA

CARL T. JAVERT, M.D., NEW YORK, N. Y.

(From the Department of Obstetrics and Gynecology, Cornell University Medical College, and the New York Hospital)

AN INCREASED number of nucleated erythrocytes in the circulating blood of newborn infants has a definite significance. Starling states that nucleated red cells practically do not occur in the newborn, while Vaughn found 5 per 100 white cells in the first day of life. Parsons states that premature infants have increased numbers in direct proportion to the degree of prematurity. The writer has observed 1,023 normoblasts and 301 erythroblasts per 100 white cells in the hydrops form of erythroblastosis fetalis. Therefore the numerical determination of these cells has diagnostic value.

THE PRESENT STUDY

The venous blood of a series of 400 unselected newborn infants, including 12 twins, and 26 negro infants, was studied; and forms the basis for this report. These infants ranged from 1,080 gm. to 5,350 gm. in weight, and were born in the Woman's Clinic of the New York Hospital between January and April, 1937.

Blood was aspirated from the umbilical vein or one of its branches on the placenta and smears were made and stained by the Wright technique. Normoblasts and erythroblasts were counted, and their number expressed in terms of 100 leucocytes. No white cell counts were made, since we were interested in testing the efficacy of as simple a procedure as possible. It is to be remembered that nucleated red cells are resistant to acetic acid and would be included in the white cell count.

The average number obtained for normoblasts was 8.7, and for erythroblasts 1.1; making a total average number for nucleated erythrocytes of 9.8, or approximately 10 per 100 white cells.

The original purpose of this study was to obtain an average figure for normoblasts and erythroblasts in cord blood of normal infants in order to facilitate the hematologic diagnosis of erythroblastosis fetalis. The prediction of prematurity in infants with an increased number of these cells was anticipated.

NOTE: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

STATISTICS

The records of the 400 infants were reviewed after dividing the cases as follows:

Group I, consisting of 275 infants having less than 10 nucleated erythrocytes, serves as the control group. These infants were mature.

Group II, consisting of 125 infants having 10 or more nucleated erythrocytes in whom a greater incidence of prematurity and immaturity was found.

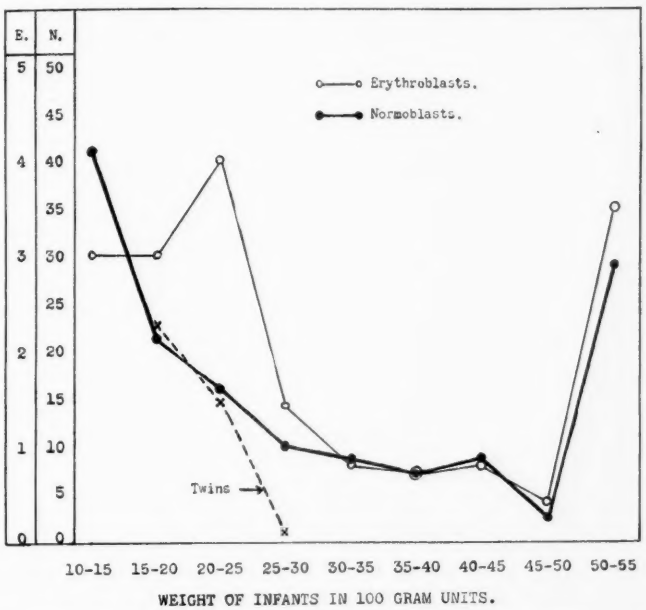

Fig. 1.—The number of erythroblasts (*E*) and normoblasts (*N*) per 100 leucocytes in relation to weight.

Sex.—There was no appreciable difference in either group.

Birth Weight.—The average weight for Group I was 3,429 gm. (7.5 pounds); while in Group II, it was 3,226 gm. (7.0 pounds); or 200 gm. less. Fig. 1 shows the average number of normoblasts and erythroblasts in relation to weight for single and twin infants. The total number of nucleated erythrocytes is less than 10 in the majority of infants weighing over 3,000 gm., and about 20 per cent had no nucleated red cells. The premature infants have an increased number.

Length.—The average crown-heel length in centimeters for Group I was 50.9, and 49.8 for Group II. Fig. 2 shows the average number of normoblasts and erythroblasts in relation to length for single and twin infants. The total number of these cells averages below 10 for infants 48 centimeters in length and over. Infants who are premature as judged by their length, have an increased number of nucleated erythrocytes.

Duration of Gestation.—The expected date of confinement as calculated after the method of Naegele was 39.9 weeks for Group I, and 39.1 weeks for Group II. Fig. 3 shows the number of normoblasts and erythroblasts in relation to the duration of pregnancy for single and twin infants. After the thirty-ninth week of gestation, the average number of nucleated erythrocytes is less than 10. The curves are not as regular as those obtained for weight and length, since the expected date is so often

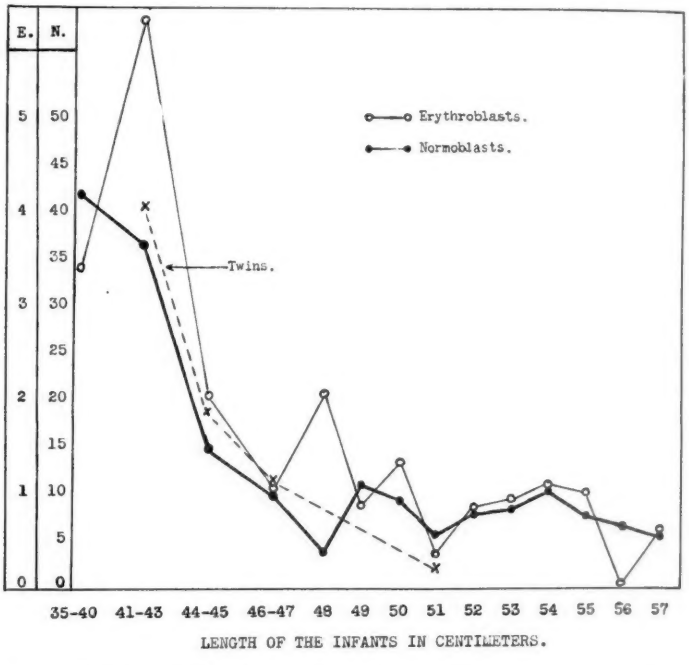

Fig. 2.—The number of erythroblasts (*E*) and normoblasts (*N*) per 100 leucocytes in relation to length.

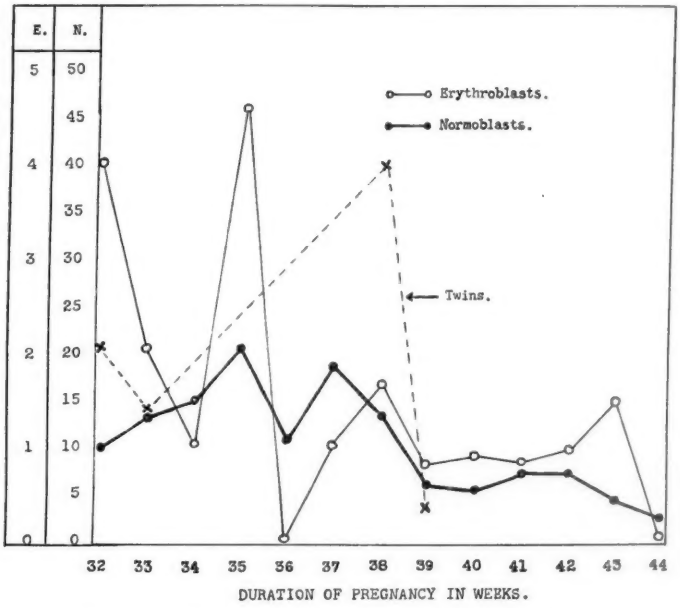

Fig. 3.—The number of erythroblasts (*E*) and normablasts (*N*) per 100 leucocytes in relation to the duration of pregnancy.

erroneous. The decline at thirty-six weeks suggests that the calculation was one month off, and that these infants were actually at term. The increased number of nucleated red cells in infants under thirty-nine weeks' gestation is significant.

Distribution of Cases.—The percentage of infants in Groups I and II in relation to weight, length, and duration of pregnancy is shown in Fig. 4. About 75 per cent of the infants in Group I were definitely mature, with an average weight of 3,429 gm., length of 50.9 cm., and duration of pregnancy of 39.9 weeks for this group. This leaves about 25 per cent of the infants, in this group considered mature by these standards, in the premature or immature group according to the blood smear examination. This graph also indicates that the nearer the period of conception,

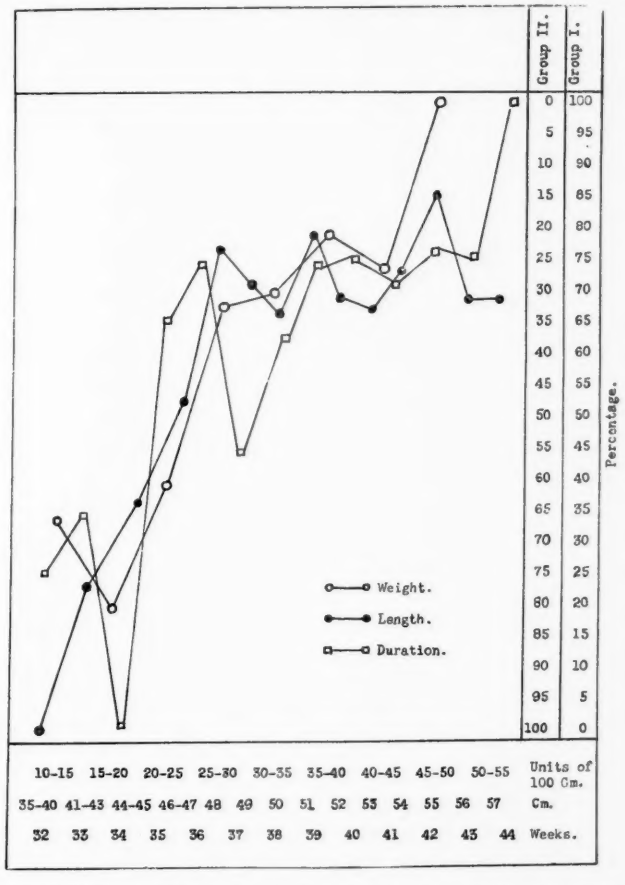

Fig. 4.—The percentage of infants in Groups I and II in relation to weight, length, and duration of pregnancy.

the higher the percentage of infants in Group II. One may conclude that the average number for nucleated erythrocytes is a helpful factor in the determination of prematurity, immaturity, and maturity. However, each case may have its individual variation from the average figure, depending on the individual degree of prematurity or maturity.

Prematurity.—Of 24 infants considered premature by the clinic standards, that is, weighing between 1,500 and 2,500 gm., and between 35 and 45 cm. in length, 8 or 33.3 per cent were in Group I, and 16 or 66.6 per cent were in Group II. This shows an increase of 100 per cent for the second group. Therefore, one-third of the infants considered premature may be mature on blood smear examination.

Twin Pregnancy.—There were 12 twin infants, and their data are presented in Table I. Their normoblastic curves have been shown in Figs. 1, 2, and 3. The curves coincide fairly well with those for single infants with regard to length and duration of pregnancy; but indicate that a twin may be mature at 2,500 gm., instead of 3,000 gm. as for the single infant. Since only 12 twins were studied, this deserves further consideration.

Twins A, B, and C, were considered mature with no fetal mortality, while Twins D, E, and F, were premature and had a mortality rate of 50 per cent. This illustrates a prognostic value for the diagnosis of prematurity and maturity by blood smear.

TABLE I. THE CONSIDERATION OF 12 TWIN INFANTS

	NORMOBLASTS	ERYTHROBLASTS	WEIGHT (GM.)	LENGTH (CM.)	DURATION (WK.)	TYPE	RESULT
				Group I			
Twins A	0	0	2,940	49	39	Double ovum	Well
	2	0	2,810	51	39		Well
Twins B	7	2	2,090	45	39	Double ovum	Well
	2	0	2,220	45	39		Well
Twins C	8	1	2,280	46	39	Double ovum	Well
	2	0	3,010	51	39	Double placenta	Well
Average	3.5	0.5	2,558	47.8	39		
				Group II			
Twins D	24	2	1,840	45	31	Double ovum	Well
	16	2	2,200	45	31		Well
Twins E	40	12	2,120	43	38	Single ovum	Dead
	40	12	1,820	44	38		Dead
Twins F	16	0	1,820	46	35	Double ovum	Well
	10	0	1,890	46	35		Dead
Average	24.3	4.6	1,948	44.8	34.5		

Negro Infants.—The 26 cases had an average weight of 3,225 gm., or 200 gm. less than the clinic average for white infants. Of these, 2 or 7.7 per cent were premature, while the clinic incidence of prematurity is about 3.5 per cent.

On blood smear examination, 12 or 46.0 per cent of the negro infants were considered premature; while 113 or 28.0 per cent of the white infants were premature on this same basis (Group II). This suggests that the higher infantile morbidity and mortality rates in the negro may be due to prematurity.

Mortality Rates.—There were 12 deaths in the 400 infants, 11 white or 2.9 per cent; and 1 negro or 3.8 per cent. This is an uncorrected figure, representing all of the stillbirths and neonatal deaths up to the fourteenth day of life due to any cause. The data are shown in Table II.

Group I consists of mature infants, according to weight, length, and duration of pregnancy, and the number of nucleated red cells, with a ratio of normoblasts to erythroblasts of 10:1. The infants in Group II are premature by these standards, and have a normoblastic-erythroblastic ratio of 6:1, if the case of erythroblastosis is omitted. Autopsy evidence confirms further that prematurity and maturity can be predicted from the blood smear.

Rate of Disappearance of Nucleated Erythrocytes.—There were 7 infants with from 14 to 190 nucleated red cells. All were normal except one, which had hemorrhagic disease of the newborn. The average weight of these infants was 3,494 gm., length 50.1 cm., and duration of gestation of 39.1 weeks. The results of daily

TABLE II. AN ANALYSIS OF THE CAUSES OF DEATH IN 12 CASES

CAUSE OF DEATH	NORMOBLASTS	ERYTHROBLASTS	WEIGHT (GM.)	LENGTH (CM.)	DURATION (WK.)
Group I					
Pre-eclampsia in mother, subarachnoid hemorrhage	0	2	2,620	53	39
Intracranial hemorrhage	6	0	3,130	50	41
Craniotomy, death in labor	9	0	3,470	50	41
Macerated fetus, cause?	6	0	3,670	56	42
Average	5.2	0.5	3,222	52	40.8
	Ratio 10:1				
Group II					
Erythroblastosis fetalis	78	32	3,070	51	33
Harelip, cleft palate, intracranial hemorrhage	32	10	2,600	48	42
Anencephaly, prematurity	40	4	1,080	40	37
Prematurity, bronchopneumonia (twin)	10	0	1,890	46	35
Prematurity	78	6	1,250	38	38
Prematurity, subarachnoid hemorrhage	20	0	2,220	44	38
Prematurity, twin	40	12	2,120	43	38
Prematurity, twin, subarachnoid hemorrhage	40	12	1,820	44	38
Average	42.2	9.5	2,006	44	37.3
Average if erythroblastosis is omitted	37.1	6.2			
	Ratio 6:1				

smears on these infants are shown in Table III. Within a period of 4 days, the nucleated forms had virtually disappeared, without specific treatment, except in the case with hemorrhagic disease which received 40 c.c. of whole blood intramuscularly and recovered.

TABLE III. THE RATE OF DISAPPEARANCE OF NUCLEATED ERYTHROCYTES IN 7 INFANTS

	NORMOBLASTS	ERYTHROBLASTS
Cord blood	69	11
Cutaneous puncture:		
First day	38	2
Second day	24	2
Third day	9	0
Fourth day	1	0

Congenital Anomalies.—These cases are tabulated in Table IV. Only 1 case is in Group I, while 7 are in Group II. This indicates that prematurity rather than the anomaly is the cause of the increased number of nucleated red cells.

Excessive Sized Infants.—Infants weighing over 4,000 gm. were classified as excessive sized infants. There were 53 such babies, with 36 or 67.9 per cent in Group I; and 17 or 32.1 per cent in Group II. Of the infants in Group II, the average number of normoblasts was 21.5, and for erythroblasts 3.0, giving a ratio of 7:1 as seen for premature infants.

As shown in Fig. 1, infants weighing over 5,000 gm. had an average of 32 nucleated erythrocytes, with a ratio of 7:1 (normoblasts to erythroblasts). While a diagnosis of prematurity in these infants (3 in number) may seem untenable, the maternal complications of diabetes mellitus, hydramnios, and multiparity, respectively are known to play a role resulting in infants of excessive size. Are they also premature?

TABLE IV. A CONSIDERATION OF 8 INFANTS WITH CONGENITAL ANOMALIES

ANOMALY	NORMOBLASTS	ERYTHROBLASTS	WEIGHT (GM.)	LENGTH (CM.)	DURATION (WK.)
Cleft palate, harelip	32	10	2,600	48	42
Anencephalic monster	40	4	1,080	40	37
Pilonidal sinus	16	2	3,190	51	40
Hypospadias, testes undescended	2	0	2,970	49	41
Umbilical hernia	20	6	3,150	50	39
Equino varus	26	2	2,660	48	40
Equino varus	28	2	3,500	54	40
Mongolian idiot	60	10	2,650	45	38
Average	28	4.5	2,725	48	39.6

Ratio of Normoblasts to Erythroblasts.—From the data in Table V, Group I has a ratio of 14:1, while Group II, which has been shown to be more premature, has a ratio of 6.6:1. Infants in Group II who are premature by weight, have a ratio of 6.5:1. The infants who were found to be premature at autopsy have a ratio of 6:1. These average ratios may be of value in addition to the actual increase in nucleated red cells.

TABLE V. THE RATIO OF NORMOBLASTS TO ERYTHROBLASTS

		NORMOBLASTS	ERYTHROBLASTS	RATIO
Group I (275 cases)		2.8	0.2	14 : 1
Group II (125 cases)		12.6	1.9	6.6 : 1
Prematurity by weight	Group I	4.3	0.4	10.8 : 1
	Group II	23.4	3.6	6.5 : 1
Twin pregnancy	Group I	3.5	0.5	7 : 1
	Group II	24.3	4.6	5.3 : 1
Excessive-sized infant	Group I	3.4	0.11	31 : 1
	Group II	21.5	3.0	7 : 1
Infantile deaths	Group I	5.2	0.5	10 : 1
	Group II	37.1	6.2	6 : 1
Erythroblastosis fetalis (3 cases) (1 case in this series)		393.0	109.0	3.3 : 1

Hemorrhagic Disease of the Newborn.—There were 5 cases in this series, giving an incidence of 1.25 per cent. These cases averaged 26.6 normoblasts and 4.6 erythroblasts, with a ratio of 6:1. This is interpreted as evidence of prematurity. The writer has reported an average number of 13 nucleated red cells in smears made on the first day of life from blood obtained by cutaneous puncture from infants with hemorrhagic disease.

Erythroblastosis Fetalis.—One case occurred in this series, giving an incidence of 1 in 400 cases. The cord smear showed 78 normoblasts and 32 erythroblasts, with a ratio of 2.5:1. This infant was delivered in the thirty-third week of gestation by cesarean section, because of premature separation of the placenta. The infant weighed 3,070 gm., was hydropic and dead-born. A diagnosis of erythroblastosis was made from the blood smear, which was substantiated by autopsy.

MATERNAL STATISTICS

The 400 maternal records were studied to determine whether other factors were also to be considered as causes of the increased number of nucleated erythrocytes in Group II. The maternal age, Wassermann reaction, parity, ante-partum weight gain, ante-partum complications, duration of labor, type of delivery, anesthesia, quinine administered

either orally or rectally, morphine and scopolamine were found to have no direct or apparent influence. Detailed analysis is omitted for lack of space. The following factors, however, deserve brief consideration.

Toxemia.—The toxemias of pregnancy were classified according to the classification of Stander and Peckham. There were 72 cases or 26.1 per cent in Group I; and 34 cases, or 27.2 per cent in Group II; showing no appreciable difference.

Anemia.—Cell volume determinations at the onset of labor as suggested by Pastore averaged 37.4 per cent and 36.6 per cent for Groups I and II, respectively, showing no significant difference.

Placenta.—The average weight of the placenta in Group I was 650 gm., and 668 gm. for Group II; which seems to indicate that weight alone is not always a criterion for prematurity. Histologic studies were made of 134 placentas by Dr. Herbert F. Traut. Of 72 placentas in Group I, 2 or 2.7 per cent showed prematurity; while of 68 placentas in Group II, 8 or 12.9 per cent were premature. This is an increase of about 400 per cent for Group II.

DISCUSSION AND SUMMARY

Prematurity has been shown to be more evident in Group II, which consists of infants having 10 or more nucleated erythrocytes per 100 leucocytes. This was seen in a slightly lower average weight, length, and duration of pregnancy, as compared with Group I. The incidence of prematurity was 100 per cent greater in Group II. This group also showed prematurity of the placenta 400 per cent more frequently. The incidence of twin pregnancy was also greater in Group II. Of the infantile deaths in Group II, 100 per cent showed prematurity at autopsy.

The study revealed the need for different standards of weight, length, duration of pregnancy, and the number of nucleated erythrocytes, for the determination of maturity and prematurity in twin infants and negro infants.

The prediction of the degree of prematurity from the number of nucleated red cells may be inaccurate in certain cases, since each infant may have an individual variation from the average figures. Some infants had abnormally high numbers and were considered at term. However this increase may be interpreted as evidence of immaturity, at least of the hemopoietic system. Thirty-two per cent of the excessive sized infants were premature according to the blood smear; and 33 per cent of the infants considered premature were mature according to the blood examination.

Prematurity is frequently associated with hemorrhagic disease, erythroblastosis fetalis, and intracranial hemorrhage. Prematurity is also more frequent in twin pregnancy. It is also associated with increased morbidity and mortality rates. Therefore accurate diagnosis of maturity and prematurity should be made in each infant from the standpoints of weight, length, duration of pregnancy, number of nucleated erythrocytes, histologic examination of the placenta, and x-ray studies of the ossification centers after the method of Adair. This will also aid in prognosis, and in the clinical management of the infant. This may be illustrated by a 1,400 gm. infant, 41 cm. long, of thirty-two weeks' gestation, who had only 6 normoblasts per 100 white cells. This infant doubled its

weight in two months, and was discharged in two months as a living "abortion." The mother presented an unclassified toxemia.

The medicolegal value of the correct determination of maturity and prematurity in cases of disputed paternity, with known date of conception, and in posthumous infants, is apparent.

An average of four days was required for the disappearance of the nucleated red cells from the circulating blood. A decrease of 100 per cent was observed on the first day of life as compared with the cord blood. This same percentage reduction is seen in the comparison of the average number of nucleated erythrocytes in the 400 infants, namely 10 per 100 white cells, and the average figure of 5 as obtained by Vaughn on the first day of life. It was my impression from several smears made simultaneously from cord blood and from cutaneous puncture, that in the latter a lower percentage of erythroblasts was found. While the difference may be due to technical error, the erythroblasts being larger probably cannot pass easily through the capillary system.

In 6 cases of erythroblastosis fetalis, the maturation period ranged from three to eleven days, with an average of six days. This is one-third longer than the average of four days stated above. Since more erythroblasts are present in this disease, a longer time is required for maturation to the normoblastic stages. The premature infant with an increased number of normoblasts, requires less time for the evolution into the nonnucleated erythrocyte. Consequently, the hematologic diagnosis of erythroblastosis and prematurity may be made most accurately from the cord blood at the time of birth.

The ratio of erythroblasts to normoblasts may be of value in the determination of prematurity, in addition to the actual increase in the number of nucleated red cells. This ratio was observed to be about 6:1 for premature infants, and from 10:1 to 14:1 for mature infants. A ratio of about 3:1 has been observed in 3 cases of erythroblastosis fetalis, which is interpreted as evidence of prematurity for this disease. Apparently the nearer the period of conception, the smaller the ratio of normoblasts to erythroblasts.

In the chorion, Stander states that blood formation can be determined in the third week. According to Arey, hemoblastic mesenchyme gives origin to megaloblasts. These primitive red blood cells are huge, having a basophilic cytoplasm, since hemoglobin is absent. Their nuclei are large, and have a lacey network, which contains several nucleoli. The megaloblasts are the precursors of proerythroblasts, and in turn erythroblasts. These cells are present in the circulation up to the second or third month of gestation, being gradually replaced by nonnucleated cells. Ryerson and Sanes observed that practically all of the erythrocytes were nucleated in early pregnancy, and that megaloblasts could be differentiated. From the third to seventh month, the liver, spleen, lymph glands, and other of the internal organs participate in blood formation, and foci of hemopoiesis are present in these organs. These foci as well as the circulating blood contain erythrocytic elements in various stages of maturation. Erythroblasts are smaller than the megaloblasts, but have similar characteristics. They mature into

normoblasts, which are still smaller, have shrunken pyknotic nuclei, and a cytoplasm that is less basophilic, since hemoglobin is being acquired. Ultimately the nonnucleated erythrocyte is produced.

As term is approached, the internal organs diminish their hemopoietic activity, and the bone marrow gradually assumes the major role of blood formation. Hemopoietic foci may persist, especially in the liver, as shown by Ferguson in 6 of 9 premature infants. The circulating blood likewise shows a decrease in the number of immature erythrocytes. Mature infants have less than 10 nucleated erythrocytes, as shown in Group I, and of these, 20 per cent had none at all.

Maturation of red cells depends on intrinsic and extrinsic factors according to Strauss and Castle, who believe that the latter may be vitamin B_2. The infant is of course dependent on the mother for these substances. The increased number of nucleated red cells in the excessive-sized infants may have been produced by a deficiency of vitamin B_2 on the basis of excessive weight gain. This is not corroborated by the twins in Group I, whose aggregate weights were excessive, namely over 4,000 gm.; without an increase in the number of nucleated red cells.

Since the completion of this study, the blood smears of 9 twin infants and 50 single infants have been evaluated, and the diagnosis of prematurity or maturity was made. The clinical records of these infants were then reviewed, and the hematologic evidence was correlated with the weight, length, and duration of gestation. From these cases, and from the original 400 cases, the following conclusions were made:

CONCLUSIONS

1. Prematurity should be considered when a smear of cord blood has 10 or more nucleated erythrocytes per 100 white cells; a mature infant is likely to have less than 10.

2. Weight, length, and the number of nucleated erythrocytes are better indices of prematurity, immaturity, and maturity, than the duration of pregnancy.

3. Twin infants and negro infants should have different standards for maturity and prematurity than single white infants.

4. Approximately one-third of the premature and excessive-sized infants, and about one-fourth of mature infants according to standards of weight and length, showed evidence of immaturity or prematurity on blood examination.

5. Infants with congenital abnormalities had an increased number of nucleated erythrocytes, which was attributed to prematurity.

6. A gradual disappearance of nucleated red cells occurs within four days after birth. Therefore the hematologic diagnosis of prematurity and erythroblastosis may be made most accurately from the cord blood.

7. The number of erythroblasts and normoblasts, as well as their ratio, seems to be approximately proportional to the degree of prematurity.

8. Routine examination of the fetal blood of the placenta is a simple diagnostic procedure.

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525 East Sixty-Eighth Street

THE EFFECT OF CALCIUM UPON UTERINE CONTRACTIONS AND UPON THE UTERINE RESPONSE TO INTRAVENOUSLY INJECTED OXYTOCICS

D. N. Danforth, Ph.D., M.B., and A. C. Ivy, Ph.D., M.D., Chicago, Ill.

(From the Department of Physiology and Pharmacology, Northwestern University Medical School)

THE literature on the relation of calcium to uterine contractility is not in agreement. In 1909 Blair Bell and Hick[1] reported in vivo experiments in which the administration of calcium as $CaCl_2$ caused marked contractions of the uterus of the pithed rabbit. In 1915 Blair-Bell[2] cited other work which led him to the conclusion that a reduction of the calcium content of the blood below an optimum level might be a factor in the causation of "primary uterine inertia"; he therefore advised the administration of calcium during the last trimester of pregnancy as prophylaxis against uterine inertia. Since the appearance of his original paper, several articles have been written on this subject, some of which[3-5] confirm the oxytocic action of calcium, while others[6-9] contradict the observations of Bell. Our investigation of the subject was undertaken because of the disagreement on this rather important subject.

The most recent report upon this subject appeared while the present work was in progress. Schübel[10] found that the minimal effective dose of pitocin was considerably diminished by the previous administration of calcium. This observation is in accord with the results to be presented in this paper.

METHODS

Twenty-five post-partum dogs and 5 post-partum rabbits were used for this study. These were allowed to deliver their young spontaneously, and twenty-four to forty-eight hours later each animal was anesthetized with nembutal and the abdomen opened. For recording the tone and motility of the uterus the method of Rudolph and Ivy[11] was employed, in which a balloon is placed in each uterine horn. The balloons were appropriately inflated and connected to a manometer. In addition a specially constructed balloon was inserted through the vagina to the level of the

cervical sphincter[12] for recording contraction of this structure. (The sphincter can be felt to contract on a finger placed in its lumen.) The abdomen was then closed with a continuous suture. The balloon at the level of the sphincter was connected to a Stoelting, aneroid-type tambour. Continuous records of the blood pressure were made with a mercurial manometer.

After the initial anesthetization, a basal anesthesia was maintained throughout the duration of the experiment by the subcutaneous injection of 1/15 to 1/5 gr. of morphine sulphate at intervals of one to two hours. This drug did not affect the uterine contractions significantly.

All of the test solutions were administered by the intravenous route. The calcium was administered as calcium chloride, in a solution such that 1 c.c. was equivalent to 30 mg. of calcium. The effect of this solution was first determined, and then, after the effect had subsided, the minimal effective doses (M.E D.) of pitocin (Parke, Davis & Co.), ergonovine (ergotrate*), and histamine (Pfanstiehl) were determined. These doses were then combined with calcium and tested.

The effect of soluble sodium hexametaphosphate, a drug (known under the trade name of Calgon), which counteracts the effect of calcium in the body, was determined, and then this drug was injected just before or along with pitocin, ergonovine, and histamine.

RESULTS

The results in both rabbits and dogs were essentially similar.

Normal.—Spontaneous activity of the uterus was recorded in all cases. The amplitude of contractions recorded on the tracing could be altered by increasing or diminishing the amount of air in the balloons, but once the proper amount of distention had been determined the contractions remained constant until some form of treatment was instituted. In most cases the cervical sphincter[12] was found to contract following the contractions of the horns; the height of the contraction of the sphincter occurred usually at the moment relaxation of the horns became complete. In some dogs the sphincter appeared to be coordinated with one horn, in others, the other horn. Variations in the same animal were not infrequent. In some cases the sphincter was found to contract irrespective of the activity of the horns, being apparently unrelated in any way to cornual activity. This was not usual in normal, untreated animals. The spontaneous motility of the uterine horns was like that reported previously.[11] In the dog the average rate of contractions was about 1 per four minutes. Between the contractions, which lasted for about one minute, both horns and sphincter were relaxed. The rate was considerably more rapid in the rabbit, an average of two full contractions occurring each minute.

The Effect of Calcium Upon the Post-Partum Uterus.—Calcium was administered in doses of 10 to 30 mg. per kilo of body weight. The essential effect upon the uterus was to increase both the tone and the rate and amplitude of contractions of both horns and cervix. This effect could be observed whether the uterus was quiescent or active. The effect was prompt, and sustained. The augmentation of activity was orderly and coordinated; spasm did not occur; slight tetany occurred in one out of 40 experiments. In one instance after contractions were inhibited by an overdose of nembutal, the administration of calcium caused an immediate return to normal rhythm. In two instances in which horns and cervix were incoordinated, the administration of calcium caused the appearance of absolute coordination. When the contractions were weak at the start of an experiment, or when they became weak after eight or ten hours of observation, the injection of calcium would frequently produce a dramatic improvement. This is illustrated by Fig. 1.

The Effect of Sodium Hexametaphosphate Upon the Post-Partum Uterus.—The injection of this drug, which combines with calcium and prevents it from manifesting its physiologic action, in adequate doses produced immediately complete quiescence even though the uterus had been extremely active prior to the injection.

*The ergotrate used in this study was generously furnished by H. W. Rhodehamel of Eli Lilly and Company.

When this drug was administered in doses of approximately 10 mg. per kilo of body weight, a depression of contractions occurred as illustrated in Fig. 2. By varying the dose different degrees of depression of uterine motility were obtained.

When the activity of the uterus was augmented by an injection of calcium, the activity could be immediately antagonized or returned to normal by the injection of an appropriate amount of sodium hexametaphosphate. This is illustrated by Fig. 3. Of course, after calcium had been injected, a larger dose of sodium hexametaphosphate was required to depress uterine motility than when calcium had not been administered.

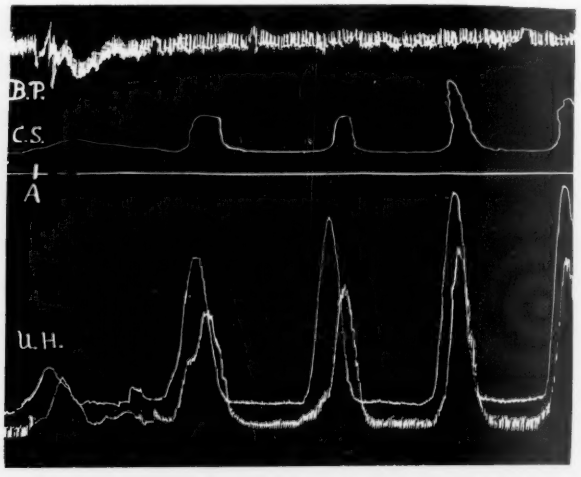

Fig. 1.—Showing the augmentation of uterine motility after calcium chloride (25 mg. per kilo) intravenously. *B. P.*, blood pressure; *C. S.*, record of the contraction of the cervical sphincter· *U. H.*, record of the contraction of the uterine horns.

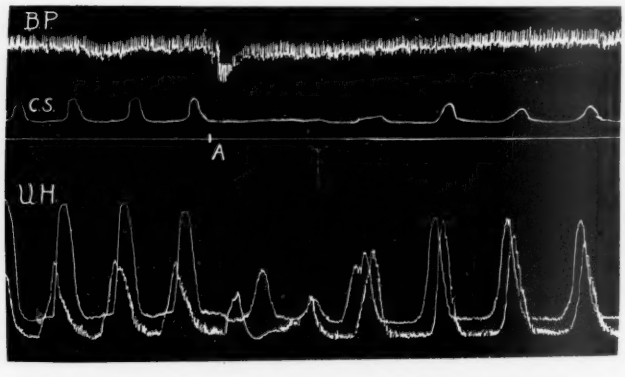

Fig. 2.—Showing the temporary depression of uterine motility by the intravenous injection of 10 mg. per kilo body weight of soluble sodium hexametaphosphate. In most animals a dose of 15 or 20 mg. caused an almost complete cessation of uterine contractions. *B. P.*, blood pressure; *C. S.*, cervical sphincter; *U. H.*, uterine horns.

The essential excitatory rôle that calcium plays in uterine motility is dramatically demonstrated by such an experiment. The results are as dramatic and almost as prompt as titrating acid against alkali. One who makes or observes such experiments cannot doubt the conclusions reached originally by Blair-Bell. In fact, the action of calcium and its antagonist, sodium hexametaphosphate, is so uniform on the post-partum dog's uterus in situ that the experiment makes a beautiful classroom demonstration.

The Effect of Pitocin Upon the Post-Partum Uterus.—In no instance was the untreated uterus refractory to this drug. Tetany and sustained spasm could be produced at will by the administration of sufficiently large doses. The minimum effective dose (M.E.D.) was found to vary in different animals from 1 c.c. of a 1:11,000 solution per kilo to 1 c.c. of 1:1,000 solution per kilo, given intravenously. When the minimum effective dose was administered to untreated animals, an increase in rate of contractions, and sometimes in amplitude, always followed. The contractions resulting were regular and showed no tendency toward incoordination or spasm. In some instances previously poor coordination was definitely improved. With the minimum effective dose the effect was usually transient and did not last more than from fifteen to twenty minutes. The cervical sphincter reacted as did the horns. The effect of pitocin was prompt and, if given immediately after a contraction, it generally caused another contraction before the usual latent period had expired.

The minimum effective dose of pitocin was determined for each animal because it was desired to determine the effect of calcium and sodium hexametaphosphate on the minimum effective dose of pitocin. These results will be mentioned later.

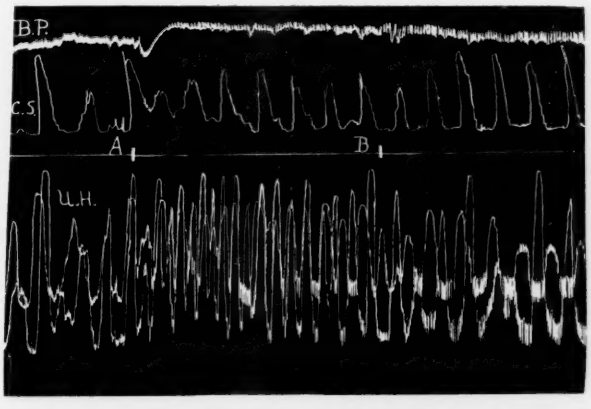

Fig. 3.—Showing a marked increase in the rate of uterine contractions caused by the intravenous injection of 15 mg. of calcium chloride per kilo at *A* and the depressing action of 10 mg. of sodium hexametaphosphate per kilo at *B*. *B. P.*, blood pressure; *C. S.*, cervical sphincter; *U. H.*, uterine horns.

The Effect of Ergonovine (Ergotrate) Upon the Post-Partum Uterus.—The effect of ergonovine on the motor activity of the uterus of the dog has not been studied. The effect of ergonovine was similar to that of pitocin, *except* that the maximal action often did not appear until as long as five minutes after the injection, and was usually maintained for a much longer period, in some instances for one hour or more. The minimum effective dose was found to vary from 1 c.c. of a 1:900 solution per kilo to 1 c.c. of a 1:100 solution. *Even in a dose as high as 1:10 in a 14 kilo dog, however, tetany and spasm of the uterus was not produced,* and only rhythmic contractions of increased rate and amplitude occurred. With still larger doses, prolonged spasm was observed only occasionally. These results on the dog confirm those for the human uterus as observed by Davis and others,[13] and Dudley and Moir.[14]

The Effect of Histamine Upon the Post-Partum Uterus.—The effect of histamine on the post-partum uterus of animals has not been studied. Histamine was administered in doses of 0.0081 mg. of the acid phosphate per kilo of body weight. This dosage was found to cause a barely perceptible change in blood pressure.

The administration of histamine in this dosage was followed, in most instances, by an increase in both rate and amplitude of contractions. Coordination and regu-

larity between the two horns was usually not affected. In some instances the sphincter apparently did not react to this treatment at all, and was caused to become incoordinated with cornual activity. This was not the rule, however, and an increase in rate and amplitude of the cornual contractions was usually accompanied by a similar change in sphincter activity. The effect of histamine was prompt, and was observed to last for anywhere from four to twenty minutes. Thus, as might have been predicted from observations made on uterine strips, histamine increases uterine motility when given in doses that do not significantly alter blood pressure. Adair and Davis[15] found that the effects of histamine upon the human puerperal uterus were questionable. This, of course, does not mean that histamine in adequate dosage will not cause the human uterus to contract, since in the dog a somewhat larger dose can be used, and the recording apparatus is more sensitive.

The Effect of Pitocin, Ergonovine (Ergotrate) and Histamine When Administered With, or Directly After, the Injection of Calcium.—When these substances were administered directly after the injection of 20 mg. of calcium per kilo of body weight, the effect upon the uterus was invariably greater than that obtained from control injections. In most instances both rate and amplitude of contractions were affected, and the cervix and horns reacted alike. Thus, calcium not only augments

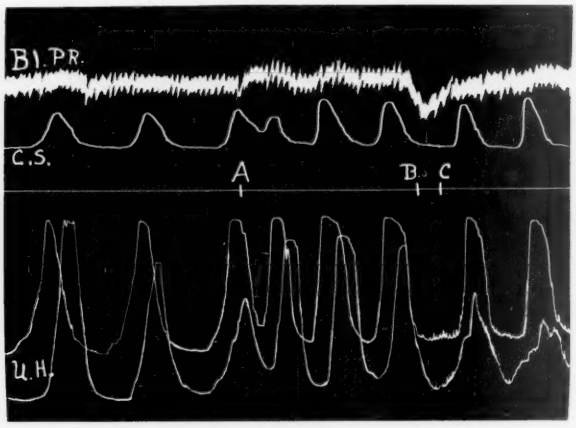

Fig. 4.—Showing abolition of the effect of pitocin on the uterus in situ by the injection of sodium hexametaphosphate. *A*, 4 c.c. of 1:100 pitocin intravenously; *B*, 27 mg. per kilo of hexametaphosphate; *C*, 4 c.c. of 1:100 pitocin; weight of dog, 18 kilo.

uterine activity by itself, but also potentiates the action of oxytocic drugs. Our observations regarding the role that calcium plays in determining the reaction of the uterus to pituitrin confirm those of Van Dyke and Hastings[5] on uterine strips.

The Effect of Pitocin, Ergonovine (Ergotrate) and Histamine When Administered Directly After the Injection of Sodium Hexametaphosphate.—When a preliminary injection of sodium hexametaphosphate was made, the effect of these drugs was considerably diminished. In some instances there was no perceptible effect from doses which previously had been shown to be definitely oxytocic. A minimum effective dose of pitocin, ergonovine, and histamine was annulled by an injection of sodium hexametaphosphate. Or, when the uterus was depressed by calcium want, the effectiveness of oxytocics was diminished.

The Effect of Sodium Hexametaphosphate When Administered Directly After the Injection of Pitocin, Ergonovine (Ergotrate) and Histamine.—As indicated previously, an augmentation of uterine contractions invariably followed the administration of pitocin, and ergonovine, the amount of augmentation being proportional to the dosage. In all instances following the administration of these drugs, the uterus could be depressed or rendered quiescent by the injection of sodium hexa-

metaphosphate. The same was true in instances in which augmentation followed the injection of histamine. An illustration of the abolition of the pitocin effect by sodium hexametaphosphate is shown in Fig. 4.

Guinea Pig and Rabbit Uterus in Vitro.—Five guinea pigs in dioestrus and four rabbits which had been isolated for two months were used for this part of the experiment. The uteri from these animals were placed in oxygenated Locke's solution at 39° C. The addition of calcium caused augmentation of the contractions. The addition of pitocin (0.1 to 2.0 units added to a 50 c.c. bath) also augmented the contractions. When the two were added to the bath simultaneously an additive effect was observed. When the uterus was bathed with oxygenated, calcium-free Locke's solution, pitocin in the doses given above either had no, or only a very slight, effect. These results confirm those of Van Dyke and Hastings,[5] and are illustrated in Fig. 5.

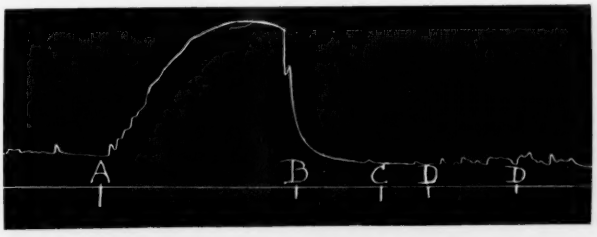

Fig. 5.—Showing the failure of the uterus of a rabbit to contract in response to pitocin when bathed by a Ca-free Locke's solution. *A*, 2 units of pitocin added to a 50 c.c. bath containing "normal" Locke's solution; *B* and *C*, uterus washed and bathed with Ca-free Locke's solution; *D*, addition of 2 units of pitocin, no response.

DISCUSSION

Our observations clearly demonstrate that calcium plays an essential role in the motor activity of the uterine musculature. When not present in adequate amounts the uterine musculature is inactive or depressed, and is refractory to the common oxytocics.

These results raise several interesting questions regarding the fundamental nature of uterine contractions. It should be remembered that calcium ions are essential constituents of all living tissue, and appear to play an important role in the permeability of the cell membrane. Soluble salts of calcium have a decided depressor effect upon striped muscle, but appear to stimulate or to be essential for the irritability of preparations of unstriped and cardiac muscle. Conversely, when the ionization of calcium is depressed by the administration of citrate or phosphate the irritability of striped muscle is increased, that of unstriped and cardiac muscle diminished. The findings which we have obtained indicate that not only is calcium concerned in determining the response of the uterus to drugs, and in the control of the irritability of the uterine musculature, but that in the relative absence of this element uterine muscle is incapable of contracting. This suggests the possibility that physiologic variations in the reactivity of uterine muscle (such as those occurring in pregnancy and at varying periods of the menstrual cycle) may result from physiologic changes in the availability of calcium ions.

In regard to the relation of this work to the problem of the onset of labor, it is well known that during pregnancy changes in calcium metabolism occur. However, relatively little satisfactory work has been directed toward a correlation of these changes with variations in uterine

motility during labor. Winkler[17] reports a decrease in the calcium percentage of the dry weight of the uterus at term but, paradoxically, he finds the irritability of the uterus to be increased by the administration of calcium. The findings of Stander[18] are interesting in this regard, especially since it is well known that (a) calcium is soluble in an acid medium and relatively insoluble in an alkaline one, and (b) calcium is mobilized from the bones in the presence of a diminished alkaline reserve. This author reported a markedly decreased CO_2 combining power (a relative acidosis) in women at term. Bussabarger, Freeman, and Ivy[18] attribute rarefaction of the bones of gastrectomized puppies partly to a relative postcibal acidosis, because an acidosis tends to mobilize calcium from the bones. If these observations are applicable, one is led to the attractive hypothesis that the increasing irritability and reactivity of the pregnant uterus are at least partially dependent upon the ionic calcium content of that organ in relation to other ions such as potassium, and that progressive ionic changes occur in the uterine musculature until the ionic concentration is optimal for the uterine response to those factors which ultimately precipitate parturition.

The observations made suggest several possibilities for clinical application. It has been shown that in every instance where the available calcium was sufficiently reduced all motility stopped, and the uterus was entirely refractory to drugs which had been shown previously to be oxytocic. This finding is significant in that it may provide an explanation of those rare instances in which the postpartum uterus appears to be refractory to oxytocics, and points to a possible means of alleviating such conditions. Also, since uterine irritability is decidedly reduced by the lowering of available calcium, it seems rational to advise the use of phosphates and possibly alkalies in conditions where the uterus appears excessively irritable, as in threatened abortion, or in tetany. Further, there is the indication that the efficiency of the commonly used oxytocics may be increased by their combination with calcium. It should be pointed out that these latter possibilities are merely assumptions based upon animal studies, and their investigation in the human being is beyond the scope of the present work.

CONCLUSIONS

1. Calcium is necessary for the maintenance of the tone, contractility and coordinated activity of the post-partum uterus of the dog and rabbit. When the available calcium is sufficiently reduced by the use of soluble sodium hexametaphosphate, uterine contractions do not occur.

2. The oxytocic action of pitocin, ergonovine, and histamine is potentiated by calcium.

3. Doses of pitocin, ergonovine, and histamine, which are normally adequate for a uterine response, are ineffective when the available calcium is diminished.

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UROLOGIC COMPLICATIONS FOLLOWING COMPLETE AND SUPRAVAGINAL HYSTERECTOMY*

A Comparative Study

A. J. Murphy, M.D., New York, N. Y.

(From the Clinic of the Woman's Hospital in the State of New York)

LESIONS of the urinary tract are one of the commonest complications following removal of the uterus. Subsequent to Kennedy's excellent article in 1930 on "The Reconstruction of the Cervical Ligaments Following Complete Hysterectomy,"[1] the number of these operations on ward patients at the Woman's Hospital increased twofold. From 1922 to 1929 there were 223 total hysterectomies, whereas during the past eight years there were 438 of these operations. With the increase in this operation more urologic complications have resulted.

Some writers, notably Spencer of London, and to a certain extent Goodall, advocate routine complete hysterectomy; while others, although not conforming to this view, have for various reasons increased their indications for the total operation. There is, however, some discussion among gynecologists as to which course to follow. It is the purpose of this paper to present a comparison of the urologic complications following each type of operation. As far as the urinary tract is concerned, it is hoped that these results may prove that routine complete hysterectomy has disadvantages.

Included in this series were the supravaginal and complete hysterectomies that were performed on ward patients at the Woman's Hospital during the past eight years, excluding however operations for carcinoma. The principal indications for these operations were uterine myomas, ovarian cysts, extensive tuboovarian disease and serious pathologic lesions of the cervix. The operations were performed by 17 members of the hospital staff, some of them by the resident staff under supervision.

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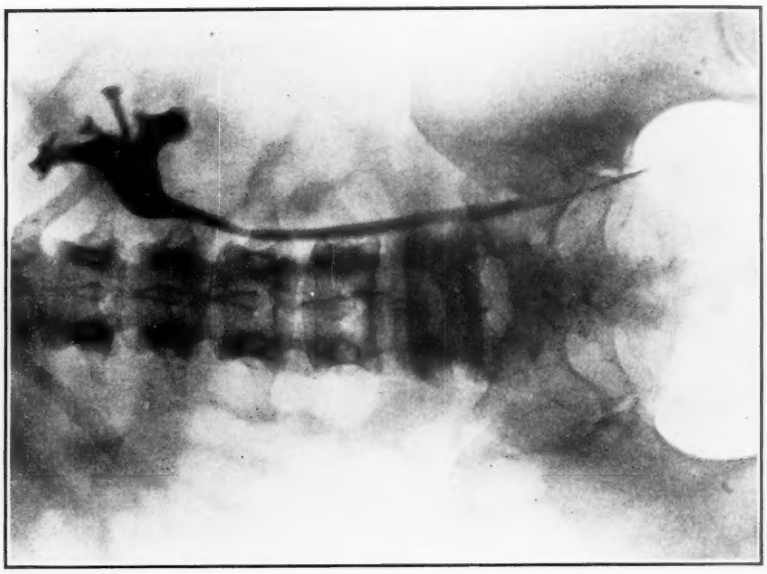
*Read at a meeting of the Gynecological Section of the Academy of Medicine, February 22, 1938.



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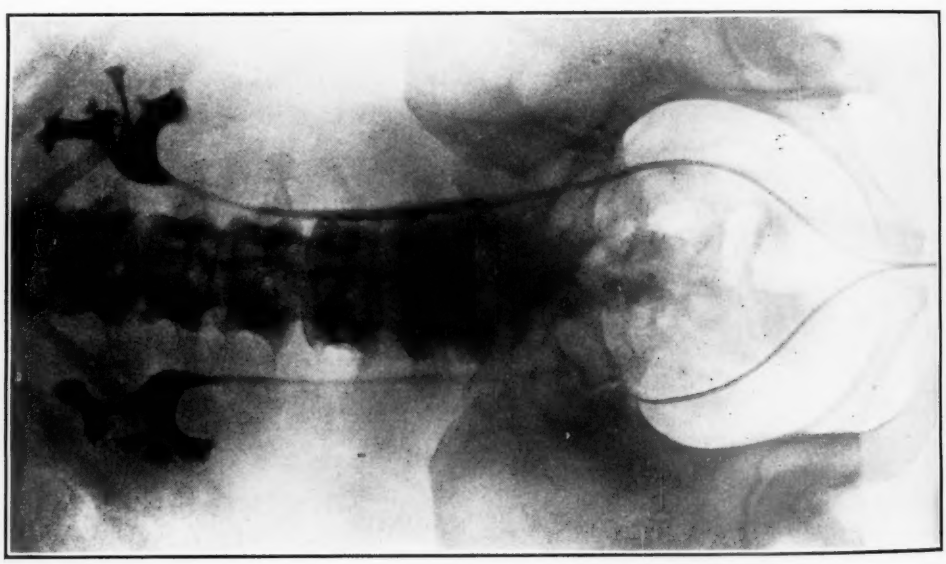


A.

Fig. 1.—*A*, Left ureteroabdominal fistula. Pyeloureterogram showing solution retained in lower ureter at the site of injury. Treated by indwelling ureteral catheter. Healed in eight days. *B*, Retrograde pyelograms taken two years later showing normal left kidney and ureter. No obstruction to ureteral catheter at injured area.

All of the complications in this group of cases were studied cystoscopically and only those unquestionable acute renal or ureteral infections were included. Those infections that were accompanied by other complications such as infected wounds, definite pelvic inflammation, phlebitis, etc., were excluded.

RENAL INFECTIONS FOLLOWING COMPLETE AND SUPRAVAGINAL HYSTERECTOMY

In the series of 1,229 supravaginal operations 47 (3.8 per cent) were complicated by an acute postoperative pyelonephritis. Following 438 complete hysterectomies there were 47 (10.7 per cent) acute renal infections or three times as many as in the previous series.

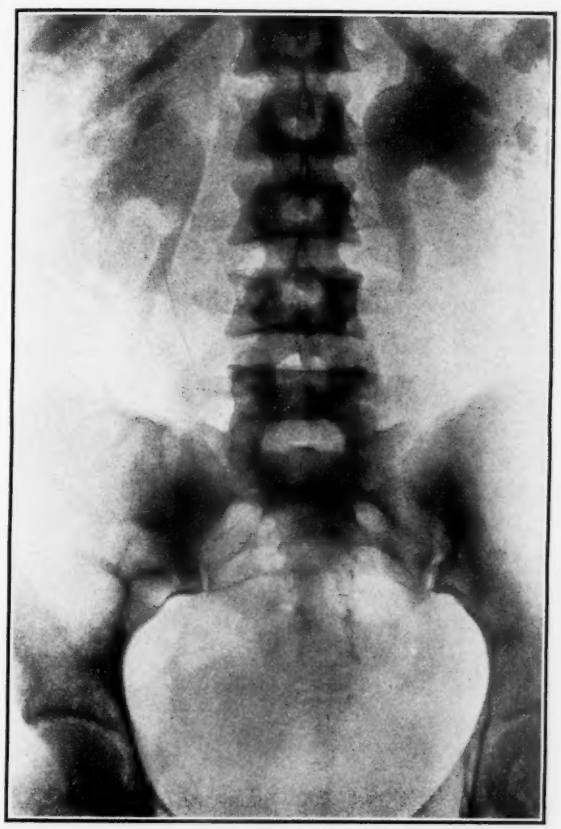


Fig. 2.—Left ureterovaginal fistula. Intravenous urogram showing ureter injured close to bladder with dilatation of left ureter above site of injury.

Although these infections may begin at any time after operation, in this series they commenced, on an average, either early, from the fifth to the seventh postoperative day, or late, from the twelfth to the fourteen day after operation. Subsequent to the supravaginal operation 34 (73 per cent) of these infections started from the fifth to the seventh day, whereas after the complete operation 37 (79 per cent) began at this time. There was no appreciable difference in the early

infections in either group regarding the urinary findings, the temperature rise, the duration of the disease, and the treatment required or the degree of hospitalization.

In the supravaginal series there were 13 (27 per cent) late infections as compared with 10 (21 per cent) in the total hysterectomy group. In 6 of the 13 infections following the subtotal operation ureteral catheter drainage from four to fifteen days was necessary, whereas it was not required in any of the late infections following the total operation. The late infections subsequent to supravaginal hysterectomy were more severe than those after complete hysterectomy. The patients had an average higher temperature of one and one-half degrees, the duration of the infection was six days longer and the average time in the hospital five days greater.

COMPLICATIONS FOLLOWING SUPRAVAGINAL HYSTERECTOMY

In this entire group there were only three ureteral traumatic complications. The bladder was accidentally opened while separating it from the anterior surface of the uterus in two patients. In each case the injury was immediately recognized and repaired, and it healed without further trouble.

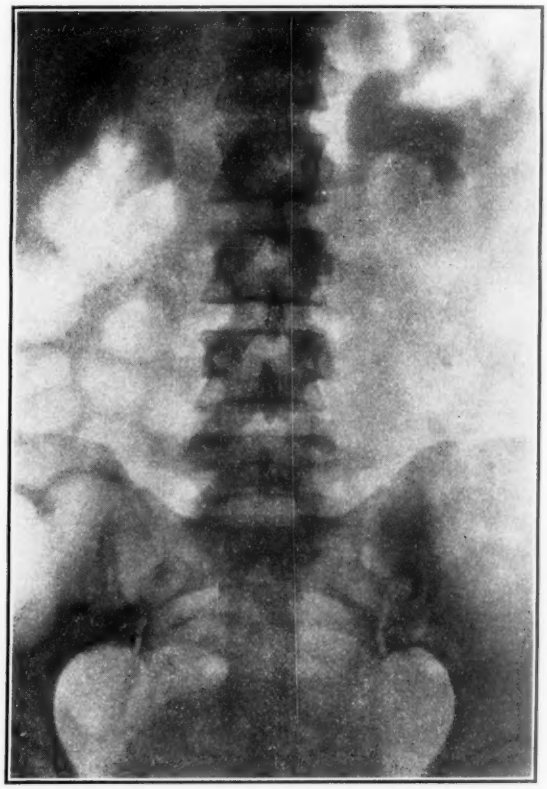


Fig. 3-*A*.

Fig. 3.—*A*, Left ureterovaginal fistula. Intravenous pyelogram shows left hydronephrosis because of ureteral injury. Patient cured of urinary leakage by destroying function of left kidney with x-ray. *B*, Intravenous pyelogram showing no function of left kidney following x-ray therapy.

The most serious complication was a left uretero-abdominal fistula. In this case (Fig. 1) the operator suspected he injured the ureter when he ligated the uterine artery. Within twenty-four hours there was urinary drainage from the abdominal wound. Cystoscopy was immediately performed and fortunately it was possible to pass a No. 5 ureteral catheter by the injured area in the ureter. This catheter was

allowed to remain in the ureter for seven days during which time the leakage of urine diminished. Eight days after operation a No. 6 catheter was easily passed up the left ureter and from this time on there was no urinary drainage from the abdominal wound. Cystoscopic study two years later showed a normal ureter and kidney.

COMPLICATIONS FOLLOWING COMPLETE HYSTERECTOMY

In this series also the bladder was accidentally opened twice but was immediately repaired and healed without further symptoms.

There were 10 serious urologic complications in the total hysterectomy group. Four patients had left ureterovaginal fistulas. One of them followed a very difficult operation for the removal of a malignant intraligamentous ovarian cyst. This patient first observed urinary leakage from the vagina thirteen days after operation. The next day a diagnosis of a left ureterovaginal fistula was made by cystoscopic study and intravenous urograms demonstrated a marked left hydronephrosis and hydroureter. This patient was cured of her fistula two months later by nephrectomy.

Fig. 3-*B*.

The second ureterovaginal fistula (Fig. 2) resulted from an operation for extensive tuboovarian disease. This patient first noticed leakage of urine eleven days after operation. Urologic study demonstrated only moderate damage to the left kidney and therefore, three months later, the ureter was transplanted into the bladder. She died of peritonitis four days after operation.

The third ureterovaginal fistula followed an operation for advanced tuboovarian disease and retroversion. This patient first noticed leakage of urine eleven days after operation. Cystoscopic study showed the fistula in the left ureter and there was also an acute infection in the kidney on that side for twenty-two days. She was observed in the follow-up clinic for several months but refused to enter the hospital for repair of the fistula and has not returned for further treatment.

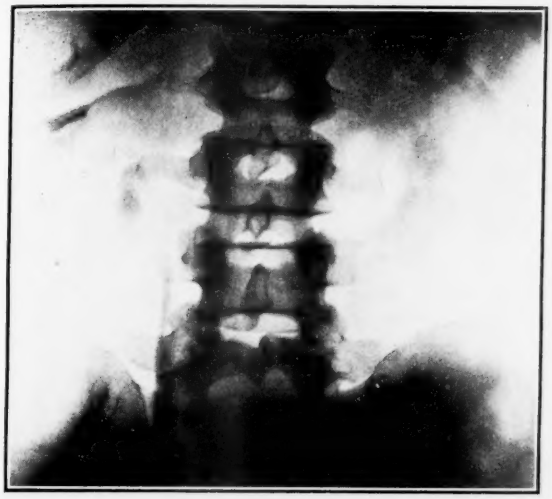
The fourth patient's fistula (Fig. 3) resulted from an operation for fibroids the size of a four and one-half months' pregnancy. She leaked urine ten days after operation and cystoscopy six days later revealed a left ureterovaginal fistula. Her urinary drainage continued for several months but because she was a poor operative risk the function of her left kidney was destroyed by x-ray therapy. Ten months after operation the urinary leakage had stopped.

The right ureter was divided in 3 patients. In 2 of these cases the injury occurred while removing an intraligamentous myoma. It was recognized at once and immediate ureterorrhaphy was done. In the third case (Fig. 4) the injury resulted from a very difficult operation for adnexal disease. It was located close to the bladder so that the ureter could be easily transplanted into that organ. These 3 patients had an uneventful postoperative recovery.

Fig. 4.—Right ureter divided while removing intraligamentous myoma. Immediately transplanted into bladder. Intravenous urogram shows only slight dilatation of right ureter and renal pelvis. Good kidney function.

There were 3 vesicovaginal fistulas in this series, and they all followed operations for uterine fibroids. Two appeared on the fourth postoperative day and 1 eighteen days after operation. Within four months all 3 patients were operated upon and cured of their fistulas.

Three patients were readmitted to the hospital with an acute pyelonephritis. Two of them were admitted eleven and fifteen days after leaving the hospital while the third entered the hospital six and one-half months after operation. Except for evidence of renal infections the cystoscopic examinations were all normal.



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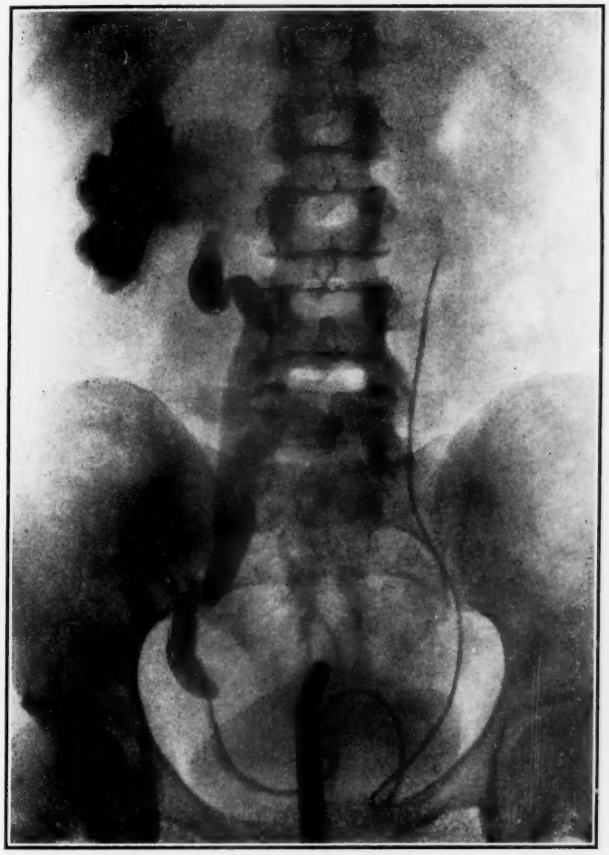

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Fig. 5.—*A*, Unsuspected injury to right ureter during supravaginal hysterectomy. Injury discovered because patient developed infection of kidney which necessitated cystoscopic study. Pyelogram shows sharply angulated right ureter. Ureter probably ligatured. *B*, Pyelogram showing dilatation of kidney and ureter following such an accident.

DISCUSSION

It is true that some of these injuries might have occurred if only a supravaginal operation had been performed. It might have happened to the two patients whose ureters were divided while removing intraligamentous tumors or to the two patients who had ureterovaginal fistulas following removal of a malignant ovarian cyst in one case and a large myoma in the other. As a rule, however, ureteral injuries that occur during a supravaginal hysterectomy are often recognized during the operation, whereas ureteral and also bladder injuries that follow the total operation usually go unrecognized and may result from necrosis due to interference with the blood supply of these organs. Despite the fact that these injuries might have followed the supravaginal operation all of these patients had a complete hysterectomy and they are included in that group.

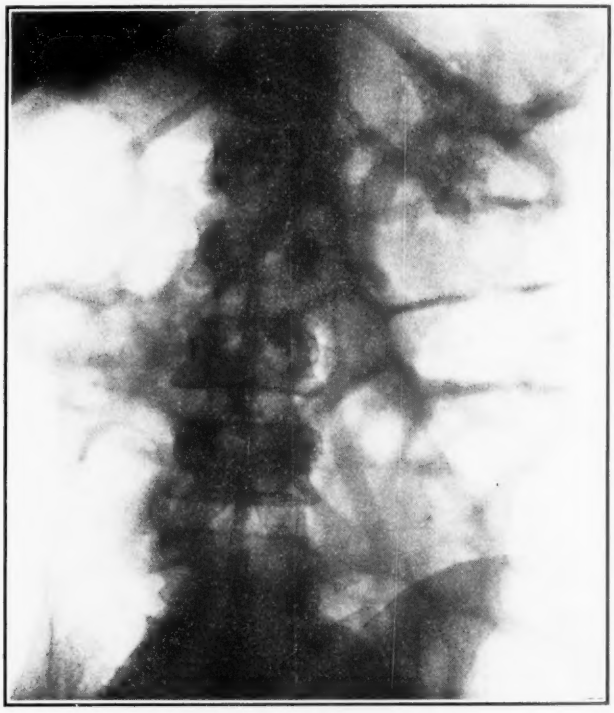

Fig. 6-*A*.

Fig. 6.—*A*, Division of right ureter during hysterectomy. Immediately repaired. Intravenous urogram showing inhibition of function of right kidney for four weeks. *B*, Intravenous pyelogram five weeks after operation showing return of function to right kidney but some dilatation of pelvis and ureter.

As previously stated the late infections following supravaginal hysterectomy were more serious than those resulting from the total operation. Why is this so? The only apparent explanation is that it is the result of inflammatory obstruction of the ureter due to infection from cutting across the cervix or from the retained cervical stump.

The majority of these injuries occurred previous to 1936 so that from now on, as our experience increases, the results will be better. On the other hand, even the most expert operators will occasionally injure the ureter, because, as set forth by Bonney, "The position of the ureter is so variable in pelvic surgery." Bland states "Despite the prevailing belief that ureteral injury is rare, I believe it to be one of the most if not the most frequent as well as the most serious accident in pelvic work." Undoubtedly ureteral injuries sometimes pass unsuspected. There may be no symptoms of ureteral injury. The first indication of injury, according to Eddy and Miller, "May be anuria, hematuria or the appearance of a fistula." Even these symptoms may be absent. The

Fig. 6-*B*.

patient may develop an acute renal infection while in the hospital and the injury be observed when she is cystoscoped (Fig. 5). Harris and Brunton state that "The effects of ureteral injury may not be observed for months or even years after operation." As in this series, some patients may develop an acute infection of the kidneys, long after operation while others complain of various urinary symptoms for a considerable time. Certainly these complications must have some relation to bladder or ureteral trauma and all of these patients should have the benefit of a cystoscopic study.

Some ureterovaginal fistulas will heal spontaneously but the majority require operative treatment. Before the patient is ready for another operation, however, considerable renal damage may be caused by the

fistula. In this event nephrostomy may temporarily preserve the function of the kidney. Then, at a later date, the ureter may be transplanted into the bladder or bowel. If grave damage to the kidney has resulted from the fistula, nephrectomy will be necessary.

There may be some impairment of renal function following ureterorrhaphy. One patient in this series (Fig. 6) who had ureterorrhaphy showed inhibition of the renal function on that side for more than four

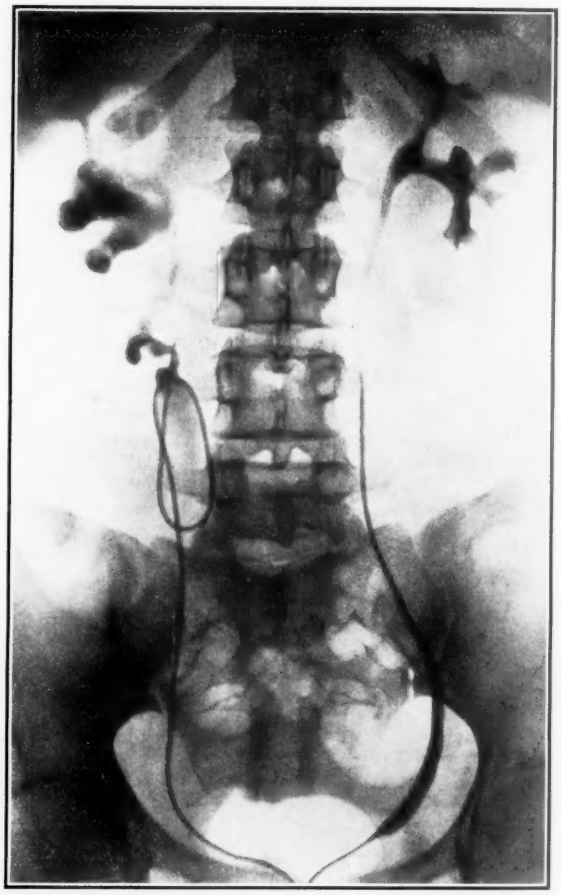

Fig. 7.—Ureter crushed by ligature during hysterectomy. Ligature removed. Cystoscopy shows large hydroureter and hydronephrosis probably because of edematous obstruction at site of injury.

weeks afterward. This resulted in a hydronephrosis which was caused by inflammatory swelling of the ureter at the site of the ureterorrhaphy. To anastomose the ureter over an indwelling ureteral catheter would tend to preserve the kidney function. In another patient (Fig. 7) whose ureter was crushed by a ligature a similar situation arose which caused a marked hydroureter and hydronephrosis. In this case, also, ureteral catheter drainage would have been advisable.

It is well known that hydronephrosis may be caused by transplantation of the ureter into the bladder as happened in one case in this

series. Hydronephrosis may also result from vesicovaginal fistulas. Those fistulas which follow complete hysterectomy are inaccessible, extremely difficult to cure and may require many operations.

From this study too, we have found that acute postoperative pyelonephritis, although three times more frequent following complete hysterectomy, is not as serious an infection as that which develops after the supravaginal operation.

In this series of cases ureteral and bladder injury was ten times more frequent following complete hysterectomy. The most serious of these injuries were the four ureterovaginal fistulas. They resulted in one death, one nephrectomy, the function of one kidney destroyed by radiotherapy and one patient who, although she could not be traced, would probably require nephrectomy in order to be cured. The seriousness of unrecognized ureteral injury with late renal complications cannot be minimized.

All of these patients were operated upon by well-trained surgeons in an outstanding hospital. Under these conditions and from the urologic viewpoint, the greater frequency of ureteral and bladder injury following complete hysterectomy, should make one hesitate before adopting this operation as a routine.

One may conclude therefore that routine complete hysterectomy is not advisable because of the greater frequency of urinary infections and ureteral and bladder injuries.

I wish to express my appreciation to Dr. Albert H. Aldridge for his valuable suggestions, to Dr. Henry G. Bugbee for the privilege of making the urologic studies and to Dr. George Gray Ward for the opportunity of presenting this paper.

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Murray, E., and Herrnberger, K.: The Functional State of the Vaginal Mucosa following Extirpation of the Uterus and Ovaries, Arch. f. Gynäk. **167:** 167, 1938.

The authors show in a series of 46 women that ovarectomy stops growth as well as the normal rhythmic changes of the vaginal mucosa. Ovarectomy with preservation of the uterus stops only the cyclic changes. Hysterectomy with ovarian conservation causes rhythmic changes which one month later give the vaginal mucous membrane the same appearance as that found during pregnancy. This is probably due to a persistent corpus luteum. Ovarectomy combined with hysterectomy produces no changes for about six weeks, after which the vaginal epithelium undergoes a progressive and finally complete atrophy. Following radiation castration, no changes can be found for about 4 months. The vaginal epithelium following castration responds readily to stimulation with estrogenic hormones and those cases which showed the most marked postoperative atrophy responded the best to hormonal stimulation. The resulting hypertrophy always is very marked. Cessation of hormonal stimulation results in further retrogression and atrophy.

Ralph A. Reis

A CRITIQUE OF THE FACTORS INVOLVED IN CESAREAN SECTION MORTALITY*

EDWARD A. SCHUMANN, A.B., M.D., F.A.C.S., PHILADELPHIA, PA.

THE use and abuse of cesarean section and its place in obstetric surgery have given rise to controversy almost since cases involving this procedure have been recorded in medical literature. During the past decade this dispute has gained impetus from the searching surveys concerning maternal mortality in general which have been carried on by obstetricians in this and other countries.

Many case series have been collected either from the larger clinics or from the studies of maternal welfare committees in cities, sometimes in states. From an analysis of these statistics it has been shown that the maternal mortality following the cesarean operation throughout the United States is 5.8 per cent, while the infant is lost in 8.5 per cent of all cases. Inasmuch as an almost 6 per cent mortality is far higher than that following comparable abdominal operations for other conditions, as for example, hysterectomy for fibroids, it has been properly felt by the profession that abdominal hysterotomy is all too often selected as a method of delivery and that the indications for its use have been broadened unwarrantably. Lynch collected the data relating to 524,117 births from various cities and states from 1930 to 1935, and found an incidence of cesarean sections of 2.5 per cent. When closely scrutinized, these figures all seem to contain a considerable factor of error. In many of the series quoted, the incidence is based upon hospital deliveries alone, which obviously does not reflect the true condition. Thus, for example, the Committee on Maternal Welfare of the Philadelphia County Medical Society in its study of maternal mortality during the years 1931, 1932, and 1933 published the cesarean section statistics of the hospitals of the city in these years. There were 68,733 hospital deliveries with a cesarean section incidence of 2.6 per cent, but without exception all of the cesarean sections done in the entire city during this period occurred in hospitals.

The total urban births for the same time were 99,579, among which were 1,775 sections, giving an incidence of the operation in relation to the total births in the area considered of 1.78 per cent, rather than the 2.6 as commonly stated.

However, it is not with the frequency with which hysterotomy is invoked that I take issue but with the statements as to the mortality consequent upon the operation. The actual number of deaths and their relative total births are unquestionably accurate, and it is not the figures which I challenge, but the deductions drawn from them.

*Read at a meeting of the Detroit Obstetrical and Gynecological Society, March 7, 1938.

In recording maternal deaths following any form of vaginal delivery, it is customary to list the mortality according to the cause. Thus deaths from eclampsia, abruptio placentae, puerperal sepsis, etc., are so catalogued, *unless* the patient undergoes a cesarean section as a method of treatment, when, should a fatality eventuate, it is at once put down as a cesarean death, the underlying cause being ignored.

For example: two women suffering from central placenta previa with massive hemorrhage are admitted to the hospital at the same time. Both are given supportive treatment, preliminary blood transfusion and the like. The obstetrician in charge of one of these patients attempts delivery by Braxton Hicks version and as a result the woman dies. The case goes on record as one of placenta previa, the version being purely secondary and considered as contributory to the fatal result. The other woman is delivered by cesarean section and also dies. This case is instantly listed as a cesarean section mortality and so appears upon the records and the group statistics without any qualifications as to the true cause of the death.

An event occurring on my service at the Philadelphia General Hospital very recently, sharply emphasized this point.

A woman was admitted in shock, with the history that forceps delivery had been attempted unsuccessfully by a private physician. A diagnosis of probable rupture of the uterus was made, and after transfusion, laparohysterotomy was performed. The uterus was found to be the seat of an extensive incomplete rupture, its cavity filled with blood and after extraction of the infant hysterectomy was performed. The patient did not survive the shock and trauma, and in the next series of case analyses appearing, this hospital will be charged with one more cesarean death, though the circumstances leading to the choice of this procedure for delivery will not be mentioned.

In order to present a clear picture of the results of abdominal hysterotomy it is necessary to return to the older classification of the elective cesarean section and the section of necessity.

In cases of the latter group, comprising as it does, all those instances of neglected dystocias, women exsanguinated as a result of placenta previa or abruptio placentae, toxemia cases which have failed to respond to conservative treatment, the mortality must of necessity be high, in direct ratio to the resistance of the patient, the extent to which infection has progressed and so on.

In the first group, that composed of elective sections performed before the onset of labor, with intact membranes and chosen as a preferred method of delivery in women with contracted pelvis, patients known to have placenta previa without present hemorrhage, and other similar indications, the mortality should be exceedingly low, comparable to that following interval appendectomy.

Fatalities following the operation should only be due to those unsuspected accidents which are an unavoidable accompaniment to any intraperitoneal surgical intervention, thrombosis, pulmonary or cerebral, rarely peritonitis and still more rarely post-partum hemorrhage.

The importance of thus dividing cases of the cesarean operation, lies not merely in presenting a true statistical picture but has a direct

bearing upon the choice of abdominal versus vaginal delivery, both as regards the obstetrician and the patient.

It is my opinion, often expressed, that in women with manifest though not necessarily insuperable disproportion, whether this be of maternal or fetal origin, elective cesarean section under local anesthesia and preferably without a preliminary test of labor, offers the best prognosis for the life and well-being of the infant as well as the subsequent health of the mother.

If one contrasts the end results of such section with those following difficult forceps delivery or version, with their constant threat of fetal intracranial hemorrhage, Erb's paralysis and the like, not to mention the permanent and often irreparable damage done to the pelvic fascias and the sacroiliac articulation of the mother, the conclusion is inevitable that hysterotomy is the procedure of choice.

The matter of the test of labor is still unsettled. Highly regarded in many clinics it is rarely utilized by the writer, who confesses to a prejudice against the procedure. If a reasonable test of labor terminates in a spontaneous or low forceps delivery, it is obvious that the obstetrician who has been considering the possibility of section in such a case has been in error as to his findings. On the other hand, all too frequently tests of labor result in dystocia requiring ultimate abdominal delivery after the patient is exhausted, the membranes ruptured, and the golden moment of election has been lost.

It is my belief that the best plan is for the obstetrician to study each patient carefully to determine finally, during the last month of pregnancy, whether the labor will proceed normally or whether severe dystocia is likely to occur. If so, he should decide upon his course of action and having determined upon it, proceed either by elective cesarean or not, as his findings indicate.

This places the responsibility for the welfare of the patient squarely upon the shoulders of the medical attendant, where it belongs. If he be a competent and trained man, his percentage of error will be small indeed.

Now to return for a moment to the question of mortality statistics as affecting the decision of doctor and patient as to whether or not abdominal hysterotomy is to be employed to effect delivery.

Assume that a young woman engages an obstetrician for her forthcoming delivery. On investigation the pelvis is found to be definitely contracted, though not to an extensive degree. As term approaches, the infant is noted to be of average or greater size and engagement does not occur satisfactorily. Abdominal hysterotomy of the elective type is suggested by the obstetrician and the patient and her husband request information as to the relative risks of abdominal versus difficult vaginal delivery.

The mortality of cesarean section according to 17 American authors as quoted by Irving runs from 1 to 8 per cent, the average for 11,491 cases being 5.8 per cent. (In the clinic of the writer at Kensington Hospital

for Women and at Chestnut Hill Hospital there have occurred in the past six years 137 cesarean sections with a maternal mortality of 4 or 2.91 per cent.)

The only authoritative information, then, which could be given to the patient in question would be that her chances of death as a result of hysterotomy would be about one in twenty or slightly less. This constitutes a formidable mortality rate and any woman is entirely justified in refusing to accept so grave a risk to her life, when vaginal delivery offers so much the better prognosis, even at the possible expense of the infant.

That the above statements portray the true situation is manifestly untrue. What then is the death rate in purely elective cesarean sections, done before the onset of labor, preferably under local anesthesia, with intact membranes, no vaginal or rectal examination having been permitted within twenty-four hours of the operation?

I am not aware of any published series of such selected cases, but from my own experience, I am convinced that the risk is minimal, certainly well under 1 per cent and comparable to the death rate in interval appendectomies and other simple intraperitoneal interventions. In support of this statement there is a summary of my last 120 *consecutive elective* sections with no maternal mortality, a surgical morbidity of 6 per cent and a total infant loss of 2 or 2.5 per cent.

Incidentally, these infant deaths were unusual. The first occurred in a woman who had previously had two babies perish during the course of spontaneous labor and a third which died one week before term. In an attempt to secure a living child, elective section was proposed and accepted and although the hysterotomy went well under local anesthesia, the child did not breathe and heart action ceased a few minutes after delivery.

In the second case the baby cried lustily at birth but perished within twenty-four hours, apparently of some congenital cardiac lesion although autopsy was not permitted to confirm this.

After such personal experience, I have no hesitation in recommending the elective operation to my patients when, in my opinion, it offers the best hope of successful delivery, and in assuring the woman and her family that the risk to mother and infant is very small.

It has been stated above that in Kensington Hospital for Women and Chestnut Hill Hospital there were four maternal deaths following cesarean section and in view of the opinions expressed previously, in this paper, it is interesting to analyze these four fatalities.

One occurred in a woman who was subjected to classical section after a twelve-hour test of labor, without vaginal examination and eight hours after rupture of the membranes. She died of a fulminating peritonitis, the fatal outcome being obviously the direct result of the operation and chargeable to it alone.

The second case was that of a woman admitted exsanguinated after hemorrhage from a central placenta previa. She was moribund and the cervix was not sufficiently dilated to permit of Braxton Hicks version. The hemorrhage continued actively and a rapid hysterectomy was performed, fluids being given intravenously during the operation. The patient perished from shock and hemorrhage within an hour. In all fairness the woman was doomed before her treatment began and the hysterectomy was certainly only a minor contributory cause to the mortality, if indeed it played any part.

The third patient was admitted in shock and coma with a vague history of having passed no urine "for some time." The bladder was dry and the diagnosis of anuria with abruptio placentae was simple. A rapid hysterotomy was done, the placenta found entirely separated and the uterus filled with blood. The woman recovered from the operation and lived for six days with practically complete suppression of urine after which she died of uremia as proved by autopsy, at which time the uterus was found to be involuting well, the hysterotomy wound healing. Here again, I think, the method of delivery had no connection with the untoward result.

The fourth case was that of a patient suffering from advanced rheumatic heart disease, who entered the hospital moribund, not in labor and having had no prenatal care. Therapeusis directed to the cardiac lesion met with no response and at the request of the patient and her family cesarean section was done in the hope of saving the child, at least. The woman perished at the completion of the operation and the infant survived but a few hours. Here was possibly an unnecessary section but certainly it played no part in the unfortunate outcome.

It appears then that of the total of these deaths following section for all causes in this institution only one could reasonably be charged to the operation; all of which seems to bear out my view as to the necessity for classifying the indication for which the cesarean section is performed before determining its responsibility in the mortality rate.

Referring again to the figures already given for two clinics at Kensington and Chestnut Hill, there were in the past six years 137 cesarean sections with a maternal mortality of 2.91 per cent. Of these operations, all of which were performed by me or one of my associates, 124 were elective and 32 were operations of necessity; many of these were carried out among seriously ill women, neglected in labor, and in a number of whom craniotomy was probably the procedure of choice. This operation, however, aside from certain religious interdictions is extremely repugnant in the presence of a living child and certain patients were undoubtedly lost by reason of our aversion to craniotomy under such circumstances.

Among the 124 elective sections, there was no maternal mortality whatsoever and a surgical morbidity of something under 6 per cent.

Among the 32 operations of necessity, there were 4 deaths, or 12.5 per cent which have already been abstracted.

This summary supports the contention that the elective operation carries with it a fairly negligible risk whereas when enforced by some complication of labor the risk is great, but is generally justified by the fact that many of these women are doomed and the hysterotomy seems to offer them and their infants the most hopeful prognosis. Again as one recalls his experiences with this operation he must be impressed by the number of instances in which section performed with no hope of success has resulted in the uneventful recovery of mother and child. Such cases, surely, seem to counterbalance the deaths which occur as a result of its employment in cases where craniotomy or other procedures of vaginal methods of delivery might have been invoked.

From the above views concerning the value of cesarean section and the relatively great safety of the elective operations, it should follow that he who holds such opinions must necessarily perform many hysterotomies. In the combined clinics summarized in this paper, during the past six years there have been 8,528 deliveries with 137 sections or an

incidence of 1.6 per cent. This is well within the group of "low cesarean clinics" and emphasizes the statement that a strong prejudice in favor of cesarean section as opposed to difficult vaginal delivery does not imply its promiscuous employment, and here I venture to become personal and to state my obstetric credo, which is: That obstetrics should be practiced by trained obstetricians, versed in all the methods and maneuvers designed to facilitate childbirth.

And also, that the obstetrician should study each patient in detail and utilize, without hesitation, that method which in his considered opinion offers the greatest hope for a successful termination of the labor as regards both mother and child.

1814 SPRUCE STREET

THE POSITION OF TOTAL HYSTERECTOMY IN THE TREATMENT OF BENIGN AND MALIGNANT CONDITIONS OF THE UTERUS*

VIRGIL S. COUNSELLER, M.D., ROCHESTER, MINN.
(From the Division of Surgery, The Mayo Clinic)

TOTAL abdominal hysterectomy has in general been considered as a radical procedure and usually has been believed to be associated with a high mortality and high morbidity; therefore, it has been regarded as a dangerous operation. In view of this generally accepted opinion, I wish to consider some indications for total hysterectomy in benign and malignant conditions, as these indications seem to be sound and essential. The most frequent benign conditions of the uterus are leiomyoma, adenomyoma, and chronic pelvic inflammatory disease.

The decision as to whether a total or subtotal abdominal hysterectomy should be performed for benign conditions is determined principally by the condition of the cervix. In cases in which hysterectomy is contemplated the cervix should be carefully inspected and palpated. Cervical erosions and lacerations, endocervicitis, cystic cervicitis and polyps all indicate an unhealthy cervix. The external os may be firm and smooth and an active endocervicitis overlooked. Cysts situated in the cervical canal may extend to the internal os and each cyst may be infected. In cases in which cervical polyps tend to recur it has been observed that malignancy is very likely to develop later. Considerable research has demonstrated that the cervix is a frequent source of infection and that such infection has a definite relation to other infectious processes within the body, such as infections of the small joints, retinitis and choroiditis. There is a very definite relationship between infections of the cervix and infections of the urinary tract as some of the lymphatics of the cervix extend directly to the base of the bladder and also upward along the ureters and to the pelvis of the kidney. A suspension of graphite injected

*Read at a meeting of the Louisiana Obstetrical and Gynecological Society, New Orleans, Louisiana, May 2, 1938.

into the cervix finds its way almost immediately to the submucosal area in the trigon of the urinary bladder. This is evidence of the paths of infection. Furthermore, a cervix which grossly appears to be normal often becomes a source of infection following a subtotal hysterectomy, as a result of interference with its normal blood supply and also because of cessation of its normal physiologic action. It is therefore not uncommon to have to remove a retained cervical stump on account of its residual inflammatory character. For these reasons it becomes an increasingly difficult problem to say what patients should be treated by subtotal hysterectomy as it is impossible to determine whether or not a cervix will continue healthy.

Since a leiomyoma is the most frequent indication for hysterectomy and as the majority of the patients who have this type of tumor have had children, it is reasonable to assume that the cervix should be removed with the uterus more often than is being done in most clinics, because it is rare to find what is considered a normal cervix in the multiparous woman.

In order to avoid some of the technical difficulties associated with total abdominal hysterectomy, a subtotal abdominal hysterectomy has been substituted and the cervix is then coned out, cauterized or even repaired or amputated. None of these methods of handling the cervix affords much protection against the later development of cancer, and also numerous infected cervical glands are often opened or only partially destroyed; this leaves an infected tissue which is prone to heal slowly and irregularly. I have seen cases in which the external os closed early before the upper portion of the cervical canal had healed; this was followed by an abscess. The infection extends to the broad ligament and cellular tissue and, therefore, contributes to a prolonged convalescence and morbidity.

Leiomyomas are often degenerative in type, and there is not only chronic infection in the cervical tissues but also much edema of the broad ligaments and of the uterosacral and ovarian ligaments. This edema is a positive sign of danger in the surgical management of these tumors. It results from lymphatic obstruction secondary to chronic infection, and, unless these tissues are removed, cellulitis will follow too frequently. Edema is also frequently encountered during the course of hysterectomy for metritis and pelvic inflammatory disease. In conditions of this type which are of long duration the infection, which usually is streptococcal in type, extends to the lymphatics of the broad ligaments and to the lymph nodes along the iliac vessels and occasionally to the inguinal regions. Unless the extent of the infection is carefully estimated, a subtotal hysterectomy may be followed by an extensive cellulitis of the broad ligaments which involves the entire pelvic tissues. The convalescence is then prolonged from three to six weeks and the cervical stump becomes fixed, edematous and painful if it is touched. This sequence of events is most likely to follow retention of the cervical stump in postabortal infections which have a tendency to exacerbations following menstruation or trauma of any type. It also is characteristic of that group of cases in which surgical interference has been previously performed dur-

ing the subacute or early stage and in which residual infection manifests itself by pain, discharge, occasional fever, and disability. Under such circumstances total abdominal hysterectomy with removal of both adnexa is the safest procedure and gives the best assurance of complete restoration of health, because all tissues that are infected are totally removed and the lymphatic involvement subsides rapidly. I am sure that subtotal hysterectomy in this group of cases is potentially a more dangerous practice and has been followed by more complications and deaths than total removal of the uterus and adnexa.

Diffuse adenomyosis, or endometriosis, of the uterus, adnexa and the peritoneum of the cul-de-sac is more satisfactorily managed by total hysterectomy when removal of the uterus is advisable. In this condition all the pelvic organs are adherent in one mass and are somewhat fixed to the intestine. The ovaries consist of chocolate cysts and the entire mass is somewhat inflammatory owing to its proximity to the sigmoid colon and rectum. In mobilizing these structures there is considerable oozing of blood, which can be most adequately controlled by ligating all branches of the uterine artery to the cervix and lateral vaginal wall followed by total removal of the uterus.

The technical difficulty of total hysterectomy under any circumstances is perhaps greatest in this condition because it is necessary to visualize the ureters and elevate the base of the bladder from the cervix. The ureters are always involved in the endometrial process and are fixed to the tissues near the cervix. It has been my custom to identify the ureters and retract them laterally by means of a gauze tape. They can later be replaced behind the peritoneum during the final peritonization of the pelvic floor, without any subsequent injury. The function of such ureters was studied in a large series of cases following total hysterectomy for these conditions, by means of intravenous urography. The ureters were found to be in their normal situation and were not dilated. It was obvious, therefore, that the ureter could withstand considerable trauma without causing subsequent complications.

When the cervix and rectum are somewhat fixed, it is often advisable to follow the suggestion of Masson, who advised that the cervix be cut across just above the uterine vessels, then, while the cervical stump is held anteriorly by a tenaculum, the rectum is separated from the posterior wall of the cervix. The cervix is then split posteriorly, and it is easy to separate it from its vaginal attachments. In these cases the healing process and the subsequent freedom from pelvic pain are truly remarkable.

Subtotal abdominal hysterectomy is not infrequently performed for benign conditions associated with an elongated cervix or in cases in which there are excessive degrees of uterine prolapse and relaxation of the vaginal walls, which later result in prolapse of the cervical stump that will require surgical treatment. In such cases it is not possible to support the cervical stump adequately or properly from the abdominal side without extensive dissection or manipulation. However, if the cervical stump is removed at the time the uterus is removed, the broad ligament,

which is the only true supporting structure, can be shortened and reattached to the sides of the vaginal vault and will afford proper support to the vagina.

The surgical risk of total hysterectomy is considered to be greater in cases of malignant lesions of the fundus than it is in cases of benign conditions, but if the patients are selected carefully there need not be any appreciable increase in the risk. As a further protection against infection the vagina must be thoroughly cleansed as there always is a bloody discharge in the vagina for some time, and this often is more or less septic. The discharge not infrequently extends into the uterine cavity. The cervix should be firmly closed by sutures to prevent soiling or contamination or the occurrence of secondary implants at the time of hysterectomy. If hysterectomy is delayed a few days in order to determine the presence or absence of malignancy in the scrapings after fixation, the surgical risk is increased greatly owing to the spread of infection from the lesion, which is usually secondarily infected, to the broad ligaments, lymphatics, and peritoneum. There must be no delay, therefore, between the curettage and the hysterectomy.

Carcinoma of the fundus is a disease which appears during or after the menopause. However, should it develop during the reproductive period of life both adnexa should be removed without regard to the physiologic effect of castration as an adenocarcinoma of the fundus not infrequently extends from the fundus along the Fallopian tube to the ovary and peritoneal cavity. It is my custom, when operating in cases of carcinoma of the fundus, to place a clamp across the fimbriated end of each Fallopian tube as soon as the abdomen is opened. The fundus of the uterus is covered with a gauze sponge and held firmly with the hand and not with instruments. The involved tissues must be handled gently to prevent dissemination of any tumor tissue to the lymphatics and to avoid rupturing the uterine wall adjacent to the malignant lesion, where it is edematous and very friable.

There are some gynecologists who favor the intrauterine application of radium and deep roentgen therapy for carcinoma of the uterine fundus instead of total extirpation of the uterus and both adnexa. I cannot agree with them for very definite reasons. First and foremost, it seems to me that a malignant lesion anywhere in the body should be removed surgically if this can be done safely and completely. If women are to have carcinoma, the fundus of the uterus is one of the most favorable sites because this organ can be totally removed with a very low mortality. In about 90 per cent of cases of malignant lesions of the fundus, the lesions grow very slowly and the grade of malignancy is 1 or 2. They remain confined to the uterus for months and occasionally for years before they spread to other tissues. The longest duration of a carcinoma of the fundus in my experience was eight years. In about 10 per cent of cases the tumor grows rapidly, the grade of malignancy is 3 or 4 and the patients are in poor condition. Symptoms usually have been present for a short time and the patients rapidly show the effects of a highly malignant tumor just as do patients with highly malignant lesions anywhere in the body. The prognosis in such cases always should be guarded. At the

Mayo Clinic we supplement surgical removal with the application of radium therapy to the vaginal vault and roentgen therapy in front and back of the pelvic region as a postoperative measure. Some physicians advise a preoperative course of radiation therapy which is followed in six to eight weeks by a panhysterectomy. It will be necessary to evaluate the results of each method in five or ten years before it is safe to say which method of treatment results in the greater number of cures. Personally I feel that this small group of highly malignant lesions offers a good field for discussion, as the results of any method or combination of methods of treatment by different gynecologists at the present time are not what we would like to have.

From the evidence so far submitted by those who advocate radium therapy for all grades of malignant lesions of the fundus, I am convinced that for the large group of low-grade lesions at least, total abdominal hysterectomy with removal of both adnexa is the preferable method of treatment.

Each year at the Clinic we are seeing a greater number of patients who have pyometria and metritis as a sequel to the intrauterine application of radium for malignancy. The result of such treatment, as far as the patient is concerned, is equally as bad as the malignant lesion. Furthermore, it is impossible to convince the patient that the cancer has most likely been destroyed. Complete relief does ensue after a panhysterectomy has been performed, but the difficulty of the operation is increased by the contraction and fixation caused by the radium therapy.

In view of the fact that carcinoma of the uterine fundus usually occurs beyond the middle period of life, there will be some cases in which physical disability is a definite contraindication to any surgical procedure. For example, extreme obesity associated with cardiovascular disease and arteriosclerosis associated with anginal attacks and senility are certainly conditions that alter the surgical risk considerably. In such cases life expectancy is not great; therefore, the patients should not be subjected to any extensive surgical procedure for malignant disease.

In evaluating the results of the treatment of carcinoma of the uterine fundus by total hysterectomy only, by irradiation only or by a combination of both methods, we found that in the five-year period from 1925 to 1929, 251 patients with cancer of the body of the uterus were treated at the Mayo Clinic. Ninety of the patients were treated by operation only; 48 were treated by irradiation only and 113 were treated by operation and irradiation. In 70.4 per cent of cases in which the carcinoma was Grade 1 and was treated by operation only, the patients were living five or more years after operation. In the 113 cases in which cancers of Grade 2 or higher were treated by operation and irradiation, 63.8 per cent of the patients were living five or more years after completion of the treatment. Of the small group of patients who were either poor surgical risks or who were considered to have inoperable lesions, 22.5 per cent were living five or more years after irradiation alone.

In this country malignant lesions of the uterine cervix generally have been considered more amenable to irradiation therapy than to surgical removal of the uterus. The explanation is that 90 per cent of the cancers

of the cervix are highly malignant lesions and extend early to contiguous structures, which makes it highly improbable that the entire growth can be removed. Also, in approximately 90 per cent of the cases the condition is inoperable at the first examination. Only about 5 to 10 per cent of the lesions have a low grade (Grade 1 or 2) of malignancy, and might be considered operable if the patients are observed early in the course of the disease. In such instances a more radical hysterectomy than the usual total abdominal hysterectomy is indicated. The Wertheim abdominal hysterectomy is usually employed; this consists not only of total removal of the uterus and adnexa but of removal of all the tissue within the broad ligaments and the upper 1 or 2 inches of the vagina. This procedure is unquestionably more difficult than the usual total hysterectomy and should be undertaken only by those who are completely familiar with the technic involved. At the Clinic our attitude with respect to surgical treatment of carcinoma of the cervix is illustrated by the fact that the condition was treated by operation in only 18 of a series of 717 cases. Six hundred and forty-two patients were treated by irradiation only, and 57 were treated by both operation and irradiation. More recently, some of the smaller lesions have been destroyed by irradiation, and six to eight weeks later a total abdominal hysterectomy is performed on the basis that the chances of cure may be increased by complete removal of the organ involved. Sufficient time has not transpired since operation to evaluate the results in the group of cases in which this method has been used.

Malignant lesions of the adnexa usually are encountered among patients who are more than thirty-five years of age, and the incidence is greatest in the fifth decade of life. The uterus may or may not be involved in the malignant process, but it may and often does contain benign lesions such as myomas and adenomyomas which necessitate removal of the uterus. The endometrium is occasionally the site of an independent malignant lesion in addition to that found in the adnexa. Malignant lesions of the ovary, such as papillary carcinomas and the solid carcinomas, become attached early to the peritoneum of the broad ligament and to the posterior surface of the uterus; therefore, if one expects to eradicate the malignant process it is necessary to remove the entire uterus as well as the adnexa. Furthermore, 50 per cent of malignant cysts affect both ovaries, and the effects of castration must be disregarded and a panhysterectomy must be performed in cases in which such lesions affect a young woman.

When malignant lesions of the adnexa involve the uterus, peritoneum, or omentum, the ultimate prognosis is poor but not entirely hopeless. These tumors have a peculiar characteristic, and this is especially true of the malignant cysts. Although they have extended to other organs, the secondary growths often subside or are held in check by removing the parent growth by a panhysterectomy and following this procedure with intensive irradiation.

The importance of total abdominal hysterectomy and removal of both adnexa in malignant lesions of the ovary and Fallopian tube when the lesion is operable cannot be overestimated. In cases in which one adnexa has been removed six or eight months previously because of a malignant

lesion, it is common to find an inoperable lesion in the remaining ovary, and metastasis. The lymphatics of the adnexa are so intimately connected with those of the uterus that it is hardly reasonable to assume that the malignancy has not extended to the adjacent tissues of the uterus and broad ligament. Recurrence frequently is seen early at the site where the ovarian vessels were divided from their connection with the uterine artery. This is presumptive evidence that the malignant process, although it grossly appeared to be confined to the ovary, had in fact extended beyond the ovary. The result is so disastrous in such cases that I am sure the interest of the patient would be better served if panhysterectomy followed by irradiation were given more consideration.

SUMMARY

The uterine cervix is generally not normal in cases of leiomyoma of the fundus of the uterus, particularly if the patients are women who have had children. It also is difficult to estimate what cervices will remain free from infection subsequent to a subtotal abdominal hysterectomy. An infected cervical stump not uncommonly is the direct focus of infection in arthritis of the small joints, and in iritis, choroiditis, and myositis. It is difficult and frequently impossible to support a prolapsed or elongated cervix properly at the time a subtotal hysterectomy is done. In metritis and chronic pelvic inflammatory disease caused by low grade streptococcal infection, a diffuse pelvic cellulitis often occurs following a subtotal hysterectomy but is rarely a complication after total hysterectomy.

Ninety per cent of the carcinomas of the fundus are adequately managed by total abdominal hysterectomy alone or combined with irradiation. Operation will be contraindicated in a small group of cases as a result of other physical disabilities. In a very few cases of carcinoma of the cervix the Wertheim type of hysterectomy may be employed; these are cases in which the grade of malignancy is low and the patients are seen early in the course of the disease.

Total abdominal hysterectomy should be given greater consideration in the management of operable malignant lesions of the adnexa, and if the grade of malignancy is 2 or higher subsequent irradiation should be employed.

Cuthbert, J. C.: The Treatment of Urinary Infections in the Puerperium, Lancet 2: 720, 1938.

The author reports, from the Queen Charlotte's Maternity Hospital, 106 cases of puerperal urinary infection, most of them complicated by a genital tract infection.

Sulfanilamide and mandelic acid therapy proved effective in *B. coli* infections. Sulfanilamide was useful in hemolytic streptococcal urinary infections while mandelic acid was effective in the presence of *Streptococcus fecalis* which appeared to resist sulfanilamide.

CARL P. HUBER.

A CRITICAL ANALYSIS OF BLOOD LOSS FOLLOWING DELIVERY*

With Special Reference to the Value of Ergotrate

Arthur M. Reich, M.D., New York, N. Y.

(From the Department of Obstetrics and Gynecology, New York University College of Medicine, and the Obstetrical and Gynecological Service of the Third [New York University] Surgical Division, Bellevue Hospital)

THE occurrence of an excessive blood loss during and after the third stage of labor might appropriately be termed, because of its serious consequences, Obstetric Enemy Number One, for no other accident or complication in obstetrics has such potential dangers or is encountered as frequently.

The present study is an investigation of the factors influencing blood loss in a series of 1,290 consecutive cases delivered on the Bellevue Obstetrical Service during the period from April, 1936 to April, 1937, with an additional report on 1,445 consecutive deliveries on the same service from April, 1937 to April, 1938. A brief preliminary survey has been made of the incidence and special causes of hemorrhage in order to gain an idea of the extent of the problem. The chief aim, however, has been to examine the effects of certain oxytocics upon the incidence and severity of post-partum hemorrhage.

The cases were consecutive except for the exclusion of patients delivered by cesarean section. The majority were delivered by an interne or medical student under the supervision of a resident, only the cases culminating in major operative procedures being directed by an attending obstetrician.

Five hundred cubic centimeters or more of blood loss has been, somewhat arbitrarily perhaps, considered by us to constitute post-partum hemorrhage. This method has the advantage of simplicity and general use, although it is perhaps less accurate than other criteria, taking into account the weight of the patient and the cell volume of the blood (Pastore). The data collected included notes on the "action of the uterus" and the measured blood loss during the third stage, with the delivery of the placenta and thereafter.

THE INCIDENCE OF POST-PARTUM HEMORRHAGE

There was a total of 136 cases classifiable as post-partum hemorrhage in the 1,290 studied, an incidence of 10.5 per cent, or when 600 c.c. is taken as the basis, 73 cases or 5.65 per cent. This compares favorably with the figures obtained by Williams of 19.5 per cent for the 500 c.c. criterion, and 13 per cent for the 600 c.c.; by Peckham of 6.1 per cent on the basis of 600 c.c.; and by Cragin, 10 per cent on

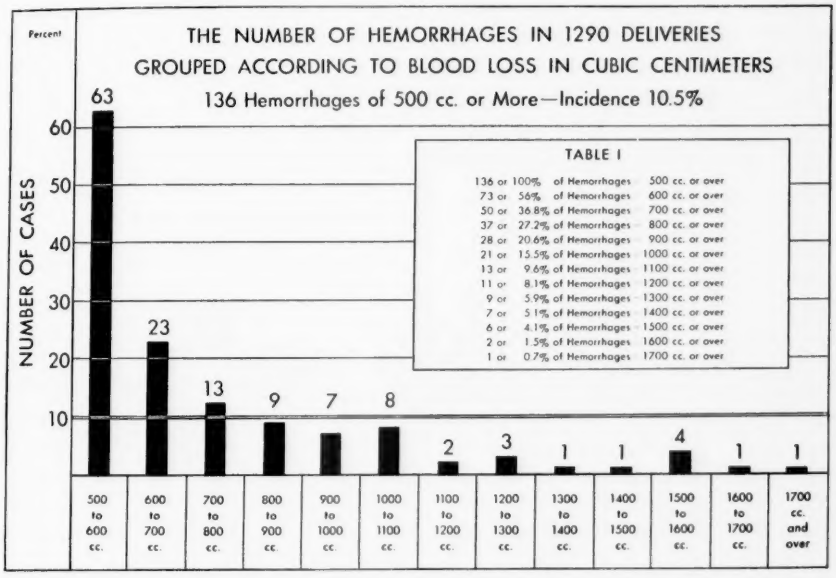
*Read before the Section on Obstetrics and Gynecology, New York Academy of Medicine, May 24, 1938.

the basis of 500; by Calkins with 2 per cent; Pastore 7.1 per cent; Litzenberg 7.1 per cent; Plass 9 per cent; all based on 600 c.c. loss. The relative similarity of these figures based on a large number of cases suggests that when much lower figures are reported the blood loss has not been correctly measured. Table I shows the number of cases in each 100 c.c. group, as well as the number and percentage of hemorrhages above each 100 c.c.

FACTORS INFLUENCING BLOOD LOSS

The hoped for effects from the introduction of a new oxytocic into obstetrics practice must naturally be restricted to the elimination of hemorrhage due to ineffective tone of the post-partum uterus. It is important to examine the causes of post-partum bleeding to determine what fraction may be influenced by a drug acting on the uterine muscle.

Under the following headings one may note certain conditions which merely predispose, but do not actually cause bleeding, such as long

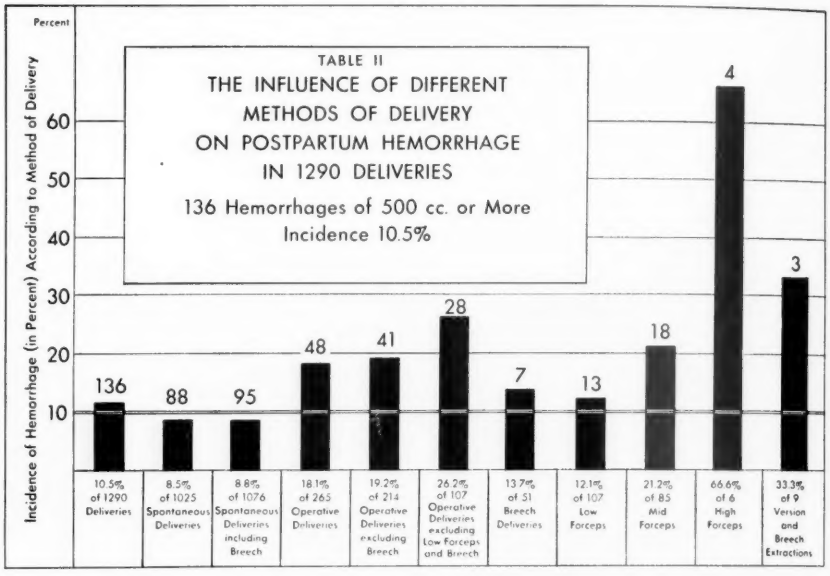

Percent
THE NUMBER OF HEMORRHAGES IN 1290 DELIVERIES
GROUPED ACCORDING TO BLOOD LOSS IN CUBIC CENTIMETERS
136 Hemorrhages of 500 cc. or More—Incidence 10.5%
NUMBER OF CASES
60
50
40
30
20
10
63
23
13
9
7
8
2
3
1
1
4
1
1
500 to 600 cc.
600 to 700 cc.
700 to 800 cc.
800 to 900 cc.
900 to 1000 cc.
1000 to 1100 cc.
1100 to 1200 cc.
1200 to 1300 cc.
1300 to 1400 cc.
1400 to 1500 cc.
1500 to 1600 cc.
1600 to 1700 cc.
1700 cc. and over
TABLE I
136 or 100% of Hemorrhages 500 cc. or over
73 or 56% of Hemorrhages 600 cc. or over
50 or 36.8% of Hemorrhages 700 cc. or over
37 or 27.2% of Hemorrhages 800 cc. or over
28 or 20.6% of Hemorrhages 900 cc. or over
21 or 15.5% of Hemorrhages 1000 cc. or over
13 or 9.6% of Hemorrhages 1100 cc. or over
11 or 8.1% of Hemorrhages 1200 cc. or over
9 or 5.9% of Hemorrhages 1300 cc. or over
7 or 5.1% of Hemorrhages 1400 cc. or over
6 or 4.1% of Hemorrhages 1500 cc. or over
2 or 1.5% of Hemorrhages 1600 cc. or over
1 or 0.7% of Hemorrhages 1700 cc. or over

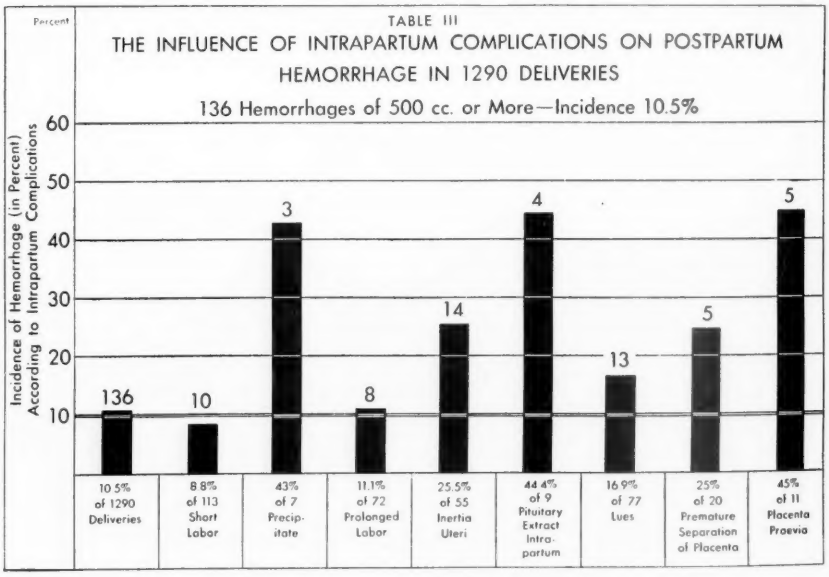
labor, large fetuses, and operative delivery. These may lead to hemorrhage either through their effect on uterine tone or through their production of injuries. The more important classifications are, therefore, the direct causes, such as lacerations and accidents to the placenta, and that of incomplete separation and the retention of a separated placenta during the third stage, as well as retained products post partum, all of these will be largely unaffected by ergotrate, while on the other hand, in post-partum uterine atony, ergotrate may influence the outcome greatly.

1. *Operations.*—(Table II.) The patient with an *operative pelvic delivery* is much more liable to a post-partum hemorrhage. In fact, when breech and low forceps were excluded, the incidence of hemorrhage in this series rose to one case out of every four, which is to be compared with an incidence of only one in twelve of the spontaneous deliveries. In the low forceps cases the incidence was about one in eight. In general, the more difficult the operative procedure, the greater was the

possibility of hemorrhage. The anesthesia, when administered inexpertly, or when prolonged, has been found to be a definite factor in increasing blood loss.

2. *Length of Labor.*—(Table III.) Prolonged labor of thirty hours or more, only slightly influenced the chance of excessive bleeding. The short labor of three hours or less diminished the notability, while with the precipitate the expectancy was high.





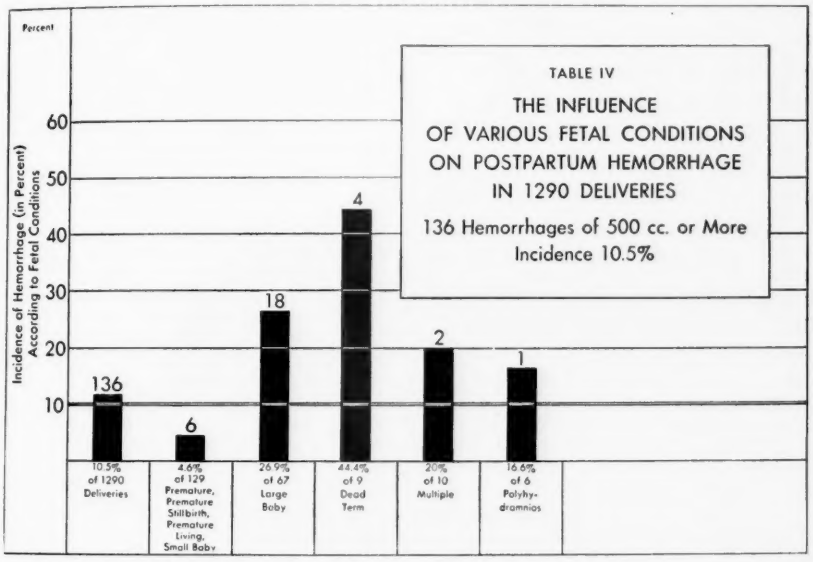
3. *Ante-Partum Uterine Tone.*—In the cases with symptoms of inertia before delivery, post-partum hemorrhage occurred in one out of every four cases. This suggests that the pathologic state is continued into the third stage, and the post-partum related to the ante-partum inertia. When pituitary extract was used intra-partum, there was a startling incidence of hemorrhage later.

4. *The size of the fetus* so frequently having a direct relationship to the size of the placenta, furnishes us with an interesting contrast. With the small baby of five pounds or less, and the premature, the risk of post-partum hemorrhage was found to be less than one in twenty-one, while with the large baby of nine pounds or more, the chances were more than one in four of excessive bleeding occurring. Those term fetuses resulting in stillbirths from a difficult labor were accompanied with a maternal hemorrhage in almost 50 per cent of the cases. Multiple pregnancy and polyhydramnios also increase hemorrhage (Table IV).

5. *Syphilis.*—The occurrence of hemorrhage in one out of six women with positive Wassermann reactions is striking enough to raise the question of the uterine pathology that causes the increased bleeding in this group. It is interesting to note also that 46.1 per cent of this group showed a puerperal infection.

6. *Parity,* per se, was without influence on the incidence of excessive bleedings.

7. *Accidents to the Placenta.*—Premature separation of the placenta with its one in four, and placenta previa with its incidence of almost one in two, were the most consistent causes of continued blood loss after the delivery.



8. *Lacerations.*—Excessive bleeding was the result of tears in 19 cases or in 13.9 per cent of the hemorrhage cases. This is a needlessly high figure since the excessive bleedings from this source are definitely in the preventable group. It would be a conservative rule to inspect cervices at once in the presence of any bleeding in those cases known or suspected to have had a rim of cervix when the delivery occurred, after labors attended with rapid and forceful progress and in cases having had manipulative procedures, as well as in multiparas with cervices known to have extensive cicatricial tissue. Yet it must not be forgotten that even episiotomies increase the blood loss. In four cases of this series the episiotomy was the principal source.

9. *The Separation of the Placenta.*—A partially detached placenta is always hazardous even after the delivery of the baby. To encourage a uterus by manipulation to contract imperfectly before retraction has taken place is to invite this accident, and in our series this abuse has tended to increase the amount and the incidence of hemorrhage. Likewise the failure to recognize and counteract a uterus whose tone is inefficient, or one which is accumulating blood within its cavity, leads to bleedings that are liable to be markedly excessive. On the other hand it must be realized that the placenta often separates completely with the first contraction or with the early contractions. Failure to recognize this occurrence, and promptly to express the foreign body represented by the detached placenta and membranes are

conducive to materially increased blood loss. The detection of the change in shape of the body of the uterus from that of discoid to globular, offers a prompt means of diagnosing complete placental separation. Often the separated placenta fails to drop at once to the lower segment, thereby obscuring the classical picture of placental separation. Too often a detached placenta is allowed to be retained, while the operator completes a plastic pelvic repair.

10. *The Expulsion of the Placenta.*—The proper expression or the Credé method of expulsion requires manipulative procedures that will tend to minimize the blood loss at this time, and is accomplished by obtaining a good uterine contraction, a correct uterine axis, avoiding trauma, and by raising the lower segment out of the pelvis. A complete placenta and membranes should be obtained, and examined for intactness. Manual removal of the partially separated placenta is a surgical procedure that should be instituted in excessive bleedings before the hemorrhage has reached an amount sufficient to present acute symptoms. It is often demanded in cases of placenta previa.

11. *The atony of the post-partum uterus* may thus often be due to errors of commission or omission, but also undoubtedly to intrinsic defects in anatomy or function of the uterine muscle. An empty uterine cavity maintained from the time of the placental delivery will remove an important factor of imperfect uterine functioning. Although possibly of value in some other conditions, notably that of incomplete separation of the placenta post partum, it is particularly in post-partum uterine inertia that we turn for help to the oxytocics.

CLINICAL STUDY OF VALUE OF ERGOTRATE

The isolation in 1934 and 1935 of a new active principle of ergot, variously termed ergometrine, ergostetrine, ergobasin, ergotocin, but chemically identical (Dudley, Thompson, Stoll, Kharasch), has led to several clinical studies, notably those of Adair and Davis, and of Moir.

In 1932 Moir proved that the efficient oxytocic action of ergot was due not to the alkaloids ergotoxine or ergotamine. He used ergot freed of these alkaloids and obtained a superior oxytocic action. It was in 1934 and 1935 that he isolated this previously undetermined substance, which he named ergometrine. All of the above named investigators as well as G. L. Brown and Sir Henry Dale are agreed that its action in the recommended therapeutic doses of 0.2 to 0.5 mg., is entirely limited to that of stimulation of the motility of the parturient and puerperal uterus through the sympathetic system, and for any further pharmacologic action the dose would need to be increased 50 times these amounts.

The special purpose of the study of these 1,290 cases was to compare the clinical value of pituitary extract, ergotamine, and ergotrate (the council accepted, ergonovine, the active principle ergotocine).

A. *The Administration of Ergotrate With the Delivery of the Anterior Shoulder.*—The first phase of this study involved the use of 1 c.c. of ergotrate (0.2 mg. or $\frac{1}{320}$ gr.) intravenously with the delivery of the anterior shoulder in vertex presentations. The cases used for control received pituitary extract 0.5 c.c. intramuscularly, after the delivery of the child and ergotamine tartrate 1 c.c. after the delivery of the placenta. Three hundred and thirty-two cases were studied, 154 with ergotrate, and 178 with the latter method.

It was found that in the ergotrate series, 86 cases or 55.8 per cent had a blood loss of *less* than 100 c.c., while with pituitary extract and ergotamine tartrate only 46 cases or 28.8 per cent bled less than 100 c.c. On the other hand no hemorrhages of over 900 c.c. were sustained with ergotrate, while 9 occurred without this drug. Six failures with ergo-

trate were noted. Three of these were due to lacerations, one to placenta previa, another occurred in a premature separation of the placenta.

Ergotrate injected intravenously acts within a minute to produce a series of contractions of the uterus which lead to a more or less tetanic state without intervals of relaxation. The placenta completely separates at once. The tone is maintained, with the surface area considerably reduced, the fundus and body of the uterus do not materially rise in the abdominal cavity. In a few cases an examining hand was placed in the uterus at the time the injection was given, and it was noted that the placenta separated, completely and with practically no blood loss, with the first contraction or about forty-five seconds after the administration of the drug. While in contrast without this drug, placental separation failed to occur within any set time, and with a varying number of contractions.

This rapid and extremely efficient reaction is not without its disadvantages, for in four cases of this group manual removal of the placenta was required due to its retention above a constriction ring in the lower uterine segment. If the ergotrate is to be given at this time as soon as the baby is delivered, it is apparently imperative to express the separated placenta promptly in order to avoid this complication. Since such perfect timing of the expression is not always possible from a practical standpoint, it was decided to try the effect of ergotrate when administered somewhat later.

B. *The Administration of Ergotrate After the Delivery of the Placenta.*—In the second part of the study one group of patients received 0.5 c.c. of pituitary extract intramuscularly after the delivery of the baby and 0.2 mg. or $\frac{1}{320}$ gr. of ergotrate (1 c.c.) intravenously after the placenta, while a control group was given pituitary extract as before, but 1 c.c. of ergotamine instead of the ergotrate, intramuscularly after the placenta. A total of 588 patients received ergotrate after the delivery of the placenta, while 548 belonged to the control group.

In this second series there were 130 patients with a blood loss of over 500 c.c., 42 or 7.1 per cent in the patients treated by ergotrate, 88 or 16.1 per cent in the patients receiving only pituitrin and ergotamine. The contrast becomes more striking when the hemorrhages in the third stage, that is to say before the administration of either ergotrate or ergotamine, are excluded; for if one considers only the late hemorrhages there were only nine after ergotrate or 1.5 per cent of the ergotrate series, but 62 after ergotamine or 11.3 per cent of the control cases.

Failures were again noted in six cases. Two of these were associated with accidents to the placenta, one and possibly others to injury.

There is, of course, a marked variation in the action of the uterine muscle after delivery even without treatment, and the normal variation is carried over into a varied response to the oxytocics. In a clinical classification of the post-partum uterine action the contraction was noted as "good" in only 28.4 per cent of the non-ergotrate group, but in the ergotrate group 89.2 per cent were noted as good. This is, of course, a rather vague classification, but the extreme hardness of the uterus after ergotrate has been given is too characteristic to leave any doubt in the

mind of anyone who has used it of its effectiveness in enhancing post-partum uterine tone. The constancy of the maintenance of uterine tone and of its effective contracture obtained throughout a period of two to three hours in the immediate post-partum uterus, affords a security against normal placental site bleedings.

C. *The Administration of Ergotrate After Hemorrhage Is in Progress.*—Although ergotrate finds perhaps its chief use in the prophylaxis of hemorrhage from post-partum uterine atony, it also has a field of usefulness in the treatment of existent hemorrhage. Ergotrate was successfully employed to stop excessive bleeding in 56 of 62 cases in which this use was attempted and pituitrin and ergotamine had failed. In three of the six failures the causes of the hemorrhage suggested local damage to uterine muscle making it unresponsive to any stimulation. Failures were again ascribable to conditions over which ergotrate would not be expected to have any influence.

D. *Ergotrate in Cesarean Section.*—Although no cases are to be here reported, ergotrate has been used in a number of cases of cesarean section on the Bellevue Service during the last two years. There is often a definite place for the administration after the delivery of the child. When it is given, the uterus above the lower segment becomes nearly bloodless, thick, and contracted. At the incised edge, the visceral peritoneum shows as a clearly defined layer. The placenta is freed from its attachment within two minutes, without bleeding from the placental site, provided the implantation is completely in the upper uterine segment. It thus affords nearly ideal conditions for a surgical closure, and, if the placental site is normally situated, the possibility of hemorrhage can be largely eliminated.

E. *Prevention of Hemorrhage as a Prophylaxis Against Infection.*—Excessive blood loss in delivery is not only a direct cause of maternal mortality, but it predisposes to later complications, notably sepsis. This was evident in a study of the present series. The total morbidity, in the 1,290 patients calculated on a standard requiring a rise to 100° on any two days after the first twenty-four hours, was 18 per cent. The morbidity among the 1,154 patients without hemorrhage was 15.1 per cent, but among the 136 patients with hemorrhage, there was the startling figure of 41.9 per cent.

A lowering of this figure may perhaps be accomplished by the more liberal use of transfusions, in the early hours of the post-partum period, to an amount closely commensurate with the loss sustained, as well as by the use of ergotrate to maintain uterine tone in the first three post-partum days. It is now in routine use on the Bellevue Service, 0.2 mg. tablets being given three times a day for the first seventy-two hours.

LIMITATIONS AND COMPLICATIONS OF ERGOTRATE THERAPY TO CONTROL POST-PARTUM BLEEDING

The action of ergotrate is, of course, exclusively upon the uterine smooth muscle. No effect may be expected when the bleeding is from any other site or when gross anatomic damage has been done to the uterine musculature. Failures have been noted by us in cases of placenta

previa with the blood coming from the relatively unresponsive lower uterine segment and in three cases of premature separation of the placenta. In two of the latter, hysterectomy was required to control bleeding, and in each, hemorrhages were found to be present throughout the musculature. Failures were also recorded in cases of placenta partially implanted in the lower uterine segment and in cases of retention of the placenta or membranes. In another unsuccessful case in which hemorrhage had also occurred after two previous deliveries, one may suppose some special endometrial lesion predisposing to bleeding. With these and perhaps a few other exceptions, hemorrhage from the placental site should not occur when ergotrate has been given.

No systemic reaction ascribable to ergotrate was noted in any patient. From our experience with the 742 cases of this series and many more since that time, we feel that the drug can be pronounced as definitely without danger to the patient. Nevertheless the occasional retention of the placenta when the drug is administered at the time of delivery of the child, appears to be a sufficient danger to make the withholding of the drug until after the placenta has been delivered advisable.

A further study of blood loss, following this control series, has been continued on all cases excluding cesarean sections, delivered at Bellevue from April, 1937 to April, 1938, 1,445 in all, during which time it has been routine to use ergotrate intravenously immediately after the placental delivery. This report and its results confirms the previous deductions (Table V).

TABLE V. AN ANALYSIS OF ALL CASES OF PATIENTS WITH POST-PARTUM HEMORRHAGE IN THE SECOND YEAR OF THIS STUDY

1,445 Consecutive Deliveries from April, 1937, to April, 1938, in Which Ergotrate, 0.2 mg. Intravenously, Was Administered After the Placental Delivery, as a Routine Procedure

			INCIDENCE
80 Patients with hemorrhage of 500 c.c.			5.37%
52 Patients with hemorrhage of 600 c.c. or over			3.5 %
CAUSES	CASES	PERCENTAGE	INCIDENCE
Uterine atony	13	16.2	0.89%
Lacerations			
Uterus, cervix, vaginal, perineal	14	17.5	
Third stage			
Incomplete separation and with delivery of placenta	48	60.0	3.3 %
Placenta previa	5	6.2	

NOTE: Of the thirteen cases of uterine atony, 3 patients had retained cotyledons and 2 had ablatio placentas, one of which necessitated a hysterectomy. This leaves 9 patients in whom ergotrate was ineffective in producing good tonicity.

DISCUSSION

It may be concluded from this second series of cases on the Bellevue Hospital Service, that uterine atony as a cause of post-partum hemorrhage has been reduced to a minimal degree, namely to an incidence of 0.89 per cent by the use of ergotrate intravenously. Also that placenta previa, low implantations of the placenta, and premature separations of the placenta, as well as the failure to secure an empty

uterus, contribute to the problem of hemorrhage after the third stage. The predisposing factors which influence excessive bleedings, showed fairly constant ratios in agreement with those analyzed in the tables of the first series. On the other hand the third stage hemorrhages are still high, namely an incidence of 3.3 per cent, and must be dealt with by proper procedures of management, as previously outlined in this paper. Lacerations in the generative tract including rupture of the uterus have taken a heavy toll, and in our series have been the cause of two maternal deaths.

The incidence of post-partum hemorrhage has been reduced 50 per cent in this second year of our study, principally as the result of the negligible occurrence of uterine atony.

CONCLUSIONS

1. Accurate collection and measurements of all blood loss not only during the third stage but for the necessary period of time thereafter, should be established on all obstetric services.

2. Certain factors preceding the third stage influence the blood loss after the delivery.

3. Hemorrhages from lacerations in the parturient canal are often undiagnosed. The incidence and the amounts lost may be high.

4. Greater consideration should be given to the conduct and management of the third stage.

5. Post-partum hemorrhage from the normally situated placental site due to imperfect contraction of the uterus is the chief theoretical indication for an oxytocic. Hemorrhages of this origin are responsible for about 70 per cent of the cases of excessive blood loss incidental to delivery.

6. In a series of 588 patients treated by the administration of ergotrate after the delivery of the placenta, the incidence of a blood loss of 500 c.c. or over was 7.1 per cent as compared with an incidence of 16.1 per cent in 548 cases in which ergotamine tartrate was given instead.

7. When only the blood loss after the third stage is considered, the incidence was 1.5 per cent in the ergotrate series and 11.3 per cent in the control series.

8. Clinical observation indicates that a profound tetanic contraction of the uterus with immediate separation of the placenta if it is still within the uterus occurs within forty-five seconds of the intravenous administration of ergotrate.

9. The use of the drug in 2,500 cases has been accompanied by no systemic reactions. The only complication that has been observed is the occasional retention of the placenta within a tightly contracted uterus when the drug is given at the beginning of the third stage.

10. Ergotrate is superior to other oxytocics in the speed, completeness, and duration of its action and has a definite place in the prophylaxis and control of hemorrhage from the normally situated placental site.

11. Puerperal infection and other morbid processes are materially influenced and dependent on the presence of large blood losses. The cell volume should be restored promptly to a normal amount by the use of transfusions in sufficient amounts.

We are indebted to Dr. John B. Pastore for the special construction of a portable Pastore blood measuring apparatus which enabled us to accurately measure blood loss.

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ETIOLOGIC FACTORS IN STERILITY*

Report of Study of One Hundred and Fifty Cases

J. Kotz, M.D., F.A.C.S., and Elizabeth Parker, M.D., A.B., M.A., Washington, D. C.

THE advent of new methods in the study of sterility and the development of new concepts of the physiology of reproduction have given a fresh impetus to the investigation of the problem of the sterile marriage. To emphasize the necessity of a complete and detailed survey of the sterile couple, it seemed that a review of the etiologic factors in a series of cases and the relation of the type and number of these factors to the results obtained after treatment might be of value.

The cases herewith reported are derived entirely from our private practice. They represent the patients who applied to us during the past four years with the primary complaint of sterility. There were 169 such cases. Ten of these did not elect to undergo the study as outlined to them, 9 patients were advised to try for a pregnancy for a longer period of time. We, therefore, had 150 cases of sterility which we were able to study completely.

METHOD OF STUDY

The methods of determining the etiologic factors in sterility have been elaborated by other investigators,[1-3] and we need not go into detail here. Suffice it to say that each investigator must establish a definite routine suitable to his own group of cases and follow it carefully in every case.

*Read at a meeting of the Washington Gynecological Society, March 26, 1938.

We have approached the problem by a complete study of the female first, adhering to the following routine: history, general physical examination, pelvic examination, complete blood count, urinalysis, Wassermann, basal metabolic rate, premenstrual blood hormone studies for estrogenic substance[4] and for gonadotropic substance,[5] premenstrual endometrial biopsy,[6-9] tubal insufflation,[10] postcoital vaginal pool examination.[11] Other procedures as x-ray, blood chemistry, etc., were resorted to when they were indicated.

CLASSIFICATION OF ETIOLOGIC FACTORS

A classification of the etiologic factors in sterility must, of necessity, be an arbitrary one since the specific factors are numerous, may occur singly or in many combinations, and assume a varying degree of importance in different cases. We have grouped these factors in large groups as follows, recognizing that with this grouping, as with any other, there is bound to be overlapping:

I. Factors in the Female
   1. Constitutional abnormalities
   2. Organic pelvic pathology
   3. Closed tubes
   4. Endocrine abnormalities

II. Factors in the Male
   1. Sexual incompetency

It is quite probable that constitutional factors do not carry the significance in sterility which is sometimes attributed to them, but they can not be ignored. Any abnormal finding on pelvic examination is important. Closed tubes are listed as a specific entity due to their frequency and importance as a cause of sterility. We have especially stressed endocrinologic investigations and have classified the evidences of glandular dysfunction as general endocrine stigmas, abnormal blood hormone levels, and abnormal endometrial patterns.

ENDOCRINE STIGMAS

General endocrine stigmas are merely findings suggestive of endocrine imbalance and are not considered to be primary causes of sterility. They include abnormalities of growth and development, menstrual irregularities, and disturbances of body metabolism. Basal metabolic rates not within the limits of the normal may be considered as a general factor since such findings occur in many types of endocrinopathies other than primary disturbances of thyroid.

ABNORMAL BLOOD HORMONE LEVELS

The premenstrual hormone tests were interpreted as follows: A positive estrogenic and a negative gonadotropic reaction is the normal finding. Complete absence of both the estrogenic and gonadotropic substance denotes primary pituitary failure. Absence of the gonadotropic substance with deficient estrogenic substance or in some instances, exces-

sive amounts of the estrogenic substance denotes partial pituitary failure. Deficient estrogenic substance with excessive amount of the gonadotropic substance indicates primary ovarian failure. The greatest value of the hormone tests is the differentiation thus obtained between primary and secondary ovarian failure. The degree of ovarian failure is best obtained by study of the endometrium.

ABNORMAL ENDOMETRIAL PATTERNS

In the normal premenstrual endometrium there is a well-differentiated secretory reaction. In our study of sterility, we have encountered several types of secretory endometria which we consider distinctly abnormal. In such cases, the glands may be fewer in number, the secretory reaction irregularly and poorly developed or there may be a mixed reaction in which some of the glands show a secretory differentiation while others are still in the follicular phase. In still another type the secretory reaction may be superimposed on an abnormal follicular reaction or associated with cystic changes in the glands. These findings, we believe, are especially important in sterility since they indicate a disturbance in the balance of the two ovarian hormones during the luteal phase of the ovarian cycle.

A more profound type of ovarian failure is evidenced by the presence of the follicular phase of the endometrium premenstrually, with or without cystic changes. Such an endometrium indicates the absence of corpus luteum function and usually anovulatory menstruation. We have found[12] that there is no distinct correlation between the type of endometrium and the character of the menstrual flow. Since this is true, these factors in sterility, abnormal hormonal balance and failure of ovulation, would be entirely missed if the endometrium is not studied.

MALE INCOMPETENCY

The diagnosis of sexual incompetency in the male was based on postcoital examination of the vaginal pool and the condom examination when necessary. Only those findings which were corroborated by the further study of a urologist are reported.

RESULTS OF STUDY

Incidence of Etiologic Factors.—The incidence of the types of sterility and the types of etiologic factors in sterility are summarized in Table I. There was an incidence of 378 for all the types of factors in the 150 cases or an average of two and one-half types of factors in each couple. Since each type may represent several abnormalities further analysis revealed an average of five and one-fifth specific factors for each couple.

Causes of Absolute Sterility.—The diagnosis of absolute sterility was made in most cases upon the presence of definite organic pathology. In no case were constitutional or endocrine factors alone the cause of the sterility although they occurred as contributing factors. There was usually one outstanding finding which could be designated as the primary cause of the sterility and which could not be remedied to restore the fertility of the patient. The specific causes were as follows: The tubes had been previously removed in 4 cases. A large fibroid uterus was present in 4 cases, in 2 of which the tubes were closed also. There was 1 case of bilateral chocolate cysts of the ovaries and one of sclerotic ovaries due to radium

castration following hydatidiform mole. There were 13 cases with closed tubes which could not be opened upon repeated inflations and in which operation was not deemed advisable or was refused by the patient. These cases with closed tubes were further complicated by the occurrence of male incompetence in 7 cases and female endocrine factors in 7 cases. Pelvic inflammatory disease with closed tubes accounted for 5 cases. There were only 2 cases in which male incompetency was the only cause.

Causes of Relative Sterility.—Relative sterility, which constituted 80 per cent of the cases studied, was found to be due in most instances to multiple factors. It is in this type of sterility that the milder degrees of abnormalities are most significant. The incidences of these factors were as shown in Table I.

TABLE I. TYPES OF ETIOLOGIC FACTORS PRESENT IN 150 CASES OF STERILITY

Absolute Sterility, 30 cases	
Primary Sterility, 18 cases	
Constitutional abnormalities	9
Organic pelvic pathology	7
Closed tubes	13
Endocrine abnormalities	8
Male sexual incompetency	9
Secondary Sterility, 12 cases	
Constitutional abnormalities	4
Organic pelvic pathology	10
Closed tubes	7
Endocrine abnormalities	3
Male sexual incompetency	4
Relative Sterility, 120 cases	
Primary Sterility, 86 cases	
Constitutional abnormalities	70
Organic pelvic pathology	35
Closed tubes	38
Endocrine abnormalities	52
Male sexual incompetency	19
Secondary Sterility, 34 cases	
Constitutional abnormalities	29
Organic pelvic pathology	17
Closed tubes	16
Endocrine abnormalities	20
Male sexual incompetency	8

Constitutional Factors.—In the relative sterilities, constitutional factors occurred 99 times with the following distribution of cases: overweight 23, underweight 15, focal infection 25, anemia 30, arrested tuberculosis 1, chronic kidney disease 2, chronic heart disease 1, goiter 2.

Pelvic Pathology.—As might be expected, the type of pelvic pathology encountered in the relative sterile group was less severe than in the absolutely sterile group. In the 52 instances of this type of factor, the conditions encountered are listed in the first columns of Table II.

Closed Tubes.—Since this condition was present in 54, or 45 per cent, of the cases of relative sterility, a search was made for significant facts in the history and examination of each which might account for the condition. In 15 cases, there was nothing found to account for the closed tubes. In the remaining cases, there were from one to four facts noted in each as possible causative factors. They were: fibroid uterus 1, pelvic inflammatory disease 16, endocervicitis 5, retroversion 7, infantile uterus 3. There was a history of gonorrhea in 10 cases and of abortion in 17 cases. Previous operation for appendicitis had been performed in 18 cases. It appears, therefore, that there is no single etiologic factor in closed tubes but that they may result from any type of acute or chronic pelvic inflammation.

TABLE II. PELVIC PATHOLOGY AS A FACTOR IN RELATIVE STERILITY

	CASES STUDIED	CASES TREATED	
		CASES PREGNANT	FAILURES
No. of cases	120	41	13
Instance of pathology	52 or 43%	19 or 46%	7 or 53%
Inflammation	17 33	4 22	5 62
Congestion	8 15	6 33	0 0
Endocervicitis	15 29	4 22	0 0
Retroversion	4 8	3 15	1 12
Fibroid	1 2	0 0	1 12
Infantile uterus	7 13	2 10	2 24

Endocrine Abnormalities.—According to our definition of endocrine factors, they were present in 72 cases. These cases were further grouped on the basis of the endometrial findings because we consider this the most accurate method of determining the state of ovarian function. Since our series dates back four years, biopsy findings were absent in 25 cases. The remaining 47 cases with endocrine factors fell into the following groups: normal premenstrual secretory endometrium 18, faulty secretory endometrium 12, follicular premenstrual endometrium 17.

In the group having a secretory endometrium the only significant findings were low basal metabolic rate in 13 cases, infantile uterus in three cases, and, one case each of oligomenorrhea and polymenorrhea. There was no instance of hormone imbalance in the blood. These cases, therefore, had normal ovarian function and the endocrine factors were of little significance.

In the group having a faulty secretory endometrium there was an increase in the incidence of other endocrine factors. Estrogenic deficiency was present in five cases. Oligomenorrhea occurred in 6 cases, polymenorrhea in 1 case, and the basal metabolic rate was below normal in 4 cases. All of these cases, therefore, represent partial secondary ovarian failure.

In the group having a follicular type of endometrium premenstrually, there was a marked increase in the associated endocrine factors. For the whole group, there were 60 specific positive findings of an endocrine nature, no case having less than two factors, 1 case had five, 8 cases had four, 7 cases had three, and 1 case had two. The hormone level was abnormal in all 17 cases, 10 having a low level of estrogenic substance and 2 having an excess of the gonadotrophic substance. Oligomenorrhea occurred in 10 cases and polymenorrhea in 2 cases. The basal metabolic rate was low in 11 cases. In all 17 cases, there were marked ovarian deficiencies, 2 of which were primary and 15 secondary.

The 25 cases in which no biopsy was done represent a heterogenous group. The blood hormone level was abnormal in 11 cases, there being 2 cases of excessive estrogenic substance, 6 of deficiency of the estrogenic substance, and 3 cases of excessive gonadotrophic substance. The basal metabolic rate was low in 12 cases. Oligomenorrhea was present in 12 cases and polymenorrhea in 1 case.

Male Incompetence.—In the cases of relative sterility male incompetence was a factor in 27 cases.

RELATION OF ETIOLOGIC FACTORS TO THE RESULTS OF TREATMENT

There is no specific routine of treatment for sterility. The one aim is to correct as many faults as possible. For the majority of the factors outlined, the methods of treatment have been well established. Our only variation which might be mentioned here is the use of x-ray to the pituitary and ovaries in the cases with disturbed function of these glands, which method we have used extensively in many types of functional disorders of the female.[13]

Of the 120 cases of relative sterility, 30 received no treatment by us. They represent patients sent for diagnostic study alone, patients who left

the city or those who did not elect to undergo the treatment outlined. Twelve patients did not follow the treatment for the prescribed time. Seventy-eight patients with relative sterility were treated. There have been 41 pregnancies, 35 of which were normal, 5 miscarriages and 1 was ectopic. There were no instances of fetal abnormalities. Thirteen cases were considered failures, and 24 patients are still under treatment.

Single-Cause Sterility.—Sterility due to a single cause is rare. Sterility due to a single type of cause occurred in only 28 cases, or 18 per cent, of the 150 cases studied. When these cases were analyzed as to specific abnormalities, the number of sterilities due to a single fault was found to be 8. Of the 28 cases, pelvic pathology accounted for 5, closed tubes 7, endocrine factors 14, and male incompetency 2. Constitutional factors did not occur alone as the cause of sterility. The total number is too small for the percentage to be significant. The most suggestive finding is that the endocrine factors constituted about one-half of the entire group and was twice as frequent as closed tubes the second most common cause. In all of the cases of endocrine dysfunction, the findings were identical, i.e., infantile uterus, follicular premenstrual endometrium and low basal metabolic rate. It would seem, therefore, for endocrine dysfunction alone to produce sterility, the glandular failure must be fairly severe.

Of the 28 patients having a single type of etiologic factor 9 received incomplete or no treatment. In the 19 patients treated there have been 12 pregnancies. The specific causative factors in the patients who became pregnant were: endocervicitis 1, pelvic congestion 1, closed tubes 4, and endocrine factors 6. The percentage of success, which is 63 per cent, is considerably higher than that of the whole group of treated patients where pregnancy occurred in 52 per cent of the patients.

Age of the Patient and Duration of the Sterility.—The age of a sterility patient when she applies for treatment is usually considered to be a significant factor. However, in the group studied, there was little variation among the different types of sterility (Table III), and all represented patients during the active reproductive stage of life. Analysis of the completely treated cases reveals that in the group in which pregnancy occurred, the average age was slightly lower and the duration of the sterility shorter. The range of the ages and duration of sterility in the successes and failures show that this rule does not always hold true. Age is important, therefore, in evaluating the significance of other factors.

Secondary Sterility.—In reviewing the previous histories of the 46 cases of secondary sterility which are summarized in Table IV, it becomes evident that the background of these patients indicates that they represent a group whose fertility is lowered irrespective of the factors operative at the time of the study. The num-

TABLE III. AGE OF PATIENT AND DURATION OF STERILITY

	NO. OF PATIENTS	AGE RANGE	AVERAGE AGE	YEARS OF STERILITY	AVERAGE DURATION OF STERILITY
Absolute Sterility:					
Primary	18	18-36	30	1-7	5.5
Secondary	12	22-37	28	2-8	4.0
Relative Sterility:					
Primary	86	19-39	27	1-18	4.0
Secondary	34	25-41	32	1-11	4.5
Patients Pregnant:					
Primary	26	20-40	27	1-18	4.0
Secondary	15	25-41	32	1-11	3.5
Failures:					
Primary	9	25-40	33	2-16	8.0
Secondary	4	25-28	31	1-7	4.0

ber of completely treated patients with secondary sterility is too small for significant analysis, but it seems that their chances of pregnancy are about equal to those of the primary sterility.

TABLE IV. PREVIOUS PREGNANCIES IN THE SECONDARY STERILITIES

	ABSOLUTE STERILITY	RELATIVE STERILITY	PATIENTS PREGNANT	TREATED FAILURE
Total No. of cases	12	34	14	4
Total pregnancies	15	49	27	8
Normal pregnancies	5	13	5	4
Spontaneous abortions	9	22	9	3
Induced abortions	0	11	12	1
Ectopic pregnancy	1	0	0	0
Prematurity	0	1	0	0
Hydatidiform mole	0	1	0	0
Eclampsia	0	1	1	0

Pelvic Pathology.—The incidence and type of pelvic pathology is summarized in Table II. Pelvic inflammatory disease accounted for the largest percentage of pelvic lesions and was the most frequent factor of those cases in which no pregnancy occurred. Endocervicitis and congestion are factors which may produce sterility but are easily corrected as shown by the fact that their incidence was high in the whole group studied and in those who became pregnant, but they were absent as a causative factor in the group of failures. Retroversion alone seems to be of little significance since pregnancy occurred in three of the four patients in whom it was present, though nothing was done to correct the retroversion. The importance of fibroids depends upon the number, size, and location of the tumors. An infantile uterus is of significance only when the endometrium indicates abnormal ovarian function.

Closed Tubes.—The incidence of closed tubes and the results of inflations are listed in Table V. Of the 54 relative sterilities with closed tubes, 36 were opened by repeated inflations. The result is probably lower than should actually be the case since the total number includes 7 patients in whom the tubes were inflated only once. Of the completely treated cases, there was an incidence of 19 closed tubes of which 16 were opened by inflation. The presence of closed tubes alone does not, therefore, render the prognosis in sterility grave. More important are the associated conditions, especially the presence of pelvic pathology which destroys the motility of the tubes and disturbs the function of the ovaries.

TABLE V. CLOSED TUBES AS A FACTOR IN RELATIVE STERILITY

	CASES STUDIED	PATIENTS PREGNANT	TREATED FAILURES
No. of Cases	120	41	13
Partially Closed Tubes:			
Number	24	6	2
Opened	18	6	2
Number of inflations	1-9	2-9	3
Average No. of inflations	3	3	3
Completely Closed Tubes:			
Number	34	8	3
Opened	18	8	0
Number of inflations	1-12	1-10	7-12
Average No. of inflations	5	6	9

Endocrine Factors.—The importance of a thorough endocrine survey is demonstrated by the frequency of occurrence of endocrine factors. Such factors were found in 72 of the total cases studied, in 23 of the patients who became pregnant and in 10 of the failures. The value of the endometrial study for diagnosis of de-

gree of ovarian failure and prognosis for therapy is evidenced by the change in ratio of success and failure with the change in the endometrium from a secretory to a follicular type of reaction as shown in Table VI. Pseudomenstruation and possibly anovulatory menstruation, occurred in 17 patients of the group with endocrine factors in which a biopsy was done, in 7 of those who became pregnant and

TABLE VI. ENDOCRINE FACTORS IN RELATIVE STERILITY

	CASES STUDIED	PATIENTS TREATED	
		PREGNANT	FAILURES
Number of patients having endocrine factors	72	23	13
Secretory endometrium	18	11	0
Abnormal secretory endometrium	12	7	2
Follicular endometrium	17	7	5
Excessive blood estrogenic substance	7	1	0
Deficient blood estrogenic and gonadotropic substance	21	11	7
Excessive blood gonadotropic substance	5	11	3
Low basal metabolic rate	40	12	5
Menstrual irregularities	34	12	7

in five of the failures. Since biopsy was not performed in some of the cases it is entirely possible that this figure should be higher, but it at least represents a minimum figure for the incidence of this condition. The blood hormone studies indicated that there were 33 cases of definite ovarian failure, 5 of which were primary in the ovary and 28 of which were secondary to other deficiencies. Of the 13 patients who became pregnant, 12 were of the secondary type and only 1 was due to the primary ovarian deficiency, while in the cases of failure there were 3 cases of primary ovarian deficiency and 7 cases of a secondary type. It would seem, therefore, that the occurrence of primary ovarian failure renders the prognosis more grave. Menstrual irregularities are merely indicative of ovarian dysfunction but are not diagnostic of the type or degree of ovarian failure. A low basal metabolic rate did not occur as the only specific endocrine cause of sterility though it was a contributing cause in more than half of the cases.

SUMMARY

In this study, the findings in 150 cases of sterility have been reviewed. It was found that in every sterile couple there was a multiplicity of factors operative. Absolute sterility was always due primarily to a specific organic pelvic pathologic condition. Relative sterility was usually due to many less serious factors. The secondary sterilities, as judged from their past histories, had a lowered fertility irrespective of the factors operative at the time of the examination.

In the relative sterilities, pelvic pathology, closed tubes, endocrine factors and male incompetence were the causes of the sterility, the significance of each being dependent upon the severity of the condition and its association with other factors. Sterility due to a single fault was rare.

Constitutional factors were not found to be the cause of sterility in any case.

Endocrine factors were found to be important in the production of sterility. Blood hormone tests are valuable in determining the etiology of ovarian failure. The endometrial biopsy is the most accurate method of determining the type and degree of ovarian failure.

CONCLUSION

There is no short cut in the management of cases of sterility. Every case must be studied diligently to determine every possible causative factor which may be present and an effort made to correct every defect which is found.

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NEONATAL MORTALITY AT THE PHILADELPHIA LYING-IN HOSPITAL*

A Seven-Year Study

Ralph M. Tyson, M.D., Philadelphia, Pa.

IN THE past thirty years great strides have been made in the reduction of infant mortality under one year of age, dropping from 166 to 53 per 1,000 live births. During this same period of time little reduction has occurred in neonatal mortality. In fact, it has been shown that the mortality of the first twenty-four hours of life has been increasing. This in all probability is due to prematurity and other related factors. In the series studied in this report, 65.5 per cent of the neonatal deaths occurred in the first twenty-four hours, and 44.7 per cent lived less than six hours.

Ten years ago the staff of the Philadelphia Lying-in Hospital began a more careful analysis of our infant deaths. All infant deaths were discussed at the monthly staff meetings and attempts were made to ascertain the circumstances concerning these deaths, and to fix individual responsibility. Errors in judgment, in technic and in methods were pointed out. The data in this report begin with April, 1930, and continue for seven years, including both private and ward cases. Particular effort was made in analyzing deaths of all babies over 4 pounds who did not have an obvious malformation. Our total mortality includes all babies for whom a birth certificate is required by the laws of the state of Pennsylvania. The age base is twenty weeks or more. Our corrected mortality was secured after babies under 4 pounds and those with obvious malformations not compatible with life were eliminated.

*Read at a meeting of the Obstetrical Society of Philadelphia, March 3, 1938.

During this period there were 15,488 deliveries (Table I), 4,062 being private or semiprivate cases. There were 944 deaths, giving a total mortality of 6.1 per cent. In the private group of 4,062 cases (Table VII) there were 98 deaths, a total mortality of 2.4 per cent. The corrected mortality considered 403 infants, 40 of which were among the private cases, giving a corrected mortality of 2.6 per cent for the entire group and 0.98 per cent for the private cases. Stillbirths accounted for 48 per cent and neonatal deaths for 52 per cent of the group; 35 babies obviously died during delivery.

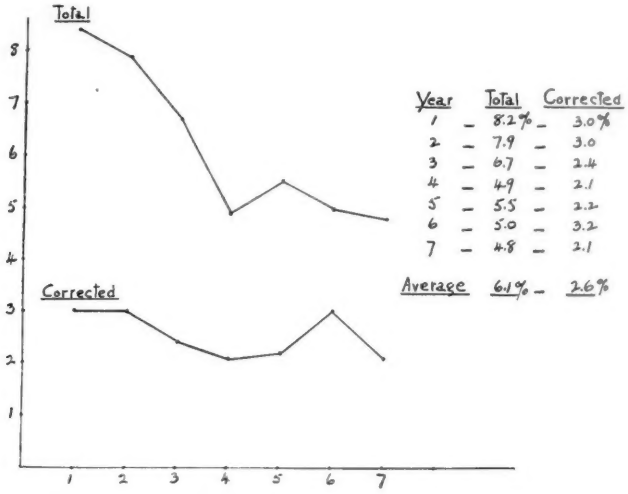

Chart 1.—Total and corrected mortality for seven years.

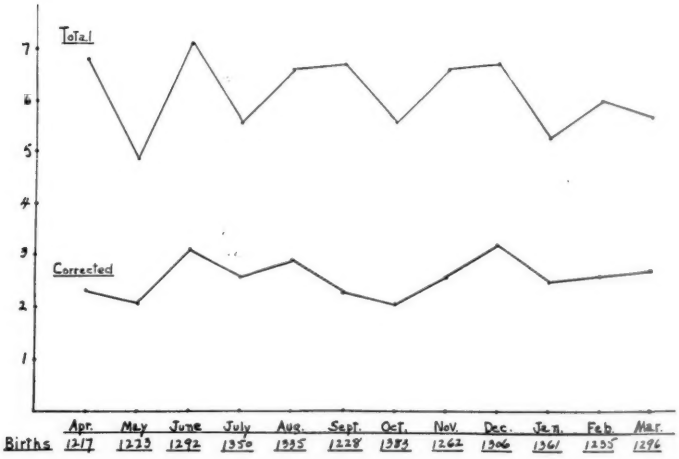

Chart 2.—Seasonal incidence.

A very interesting and satisfactory result of this study has been the steady decline in both total and corrected mortality rates, as shown graphically in Chart 1. The former dropped from 8.2 per cent to 4.8 per cent and the latter from 3 per cent to 2.1 per cent. In Chart 2, the seasonal incidence of deaths in both total and corrected groups is shown. There does not seem to be any correlation between seasonal infections

TABLE I. APRIL, 1930, TO APRIL, 1937

Total deliveries	15,488
Mortality	944— 6.1 per cent
Stillbirths	461—48.0 per cent
Deaths	483—52.0 per cent
Deaths during delivery	35
Corrected mortality	403— 2.6 per cent

and births and deaths. An enthusiastic staff with a sincere desire to improve, and working harmoniously, is perhaps the best explanation to be offered for the reduced mortality. The mature judgment of the older obstetricians and more skilled technic in handling difficult cases, perhaps accounts for the excellent results in the private cases. Closer supervision by the junior obstetric staff over the work of the residents and interns, whereby an experienced obstetrician is in attendance at all times, might be cited as another explanation.

During this period of study there were 461 stillbirths. This constitutes 48 per cent of the total deaths and is at the rate of 30 per 1,000 live births. This compares favorably with the rate for the United States for the years, 1933, 1934 and 1935, when it was, respectively, 38.9, 36.7, and 34.2.

INCIDENTAL FACTORS

A number of incidental factors are of interest in this group studied. There were 56 per cent males and 44 per cent females. This is approximately a ratio of 100 deaths in females to 127 deaths in males. Again this bears out the vulnerability of the male, which is essentially the same in other diseases, especially pneumonia. There were 61 per cent white babies and 39 per cent colored; 42 per cent of the deaths occurred in primiparas and 58 per cent in multiparas; 61 per cent of the deaths were prematures and 39 per cent were full-term children. Autopsies were secured in 594 or 63 per cent of all cases.

MULTIPLE BIRTHS

Twin deliveries during the seven-year period of study represented 2.1 per cent of the total deliveries. The influence of multiple births on neonatal mortality is shown in our records; 336 babies were the result of multiple births; 165 twin deliveries and 2 sets of triplets occurred during the seven-year study period. In 28 sets of twins both of them died; in 11 other instances one of the twins died and 1 set of triplets died. In all there were 70 deaths, or 7.4 per cent of the total deaths were associated with multiple births (Table VI). The mortality in twins is 20.3 per cent, the mortality in triplets is 50 per cent. The total mortality in multiple births is 20.8

TABLE II. BIRTH WEIGHT AND PREMATURE DEATHS

Under 2 pounds	137	505
2 to 3 pounds	140	
3 to 4 pounds	125	
4 to 5 pounds	103	
Birth weight not stated	74	
Total	579—61 per cent	

per cent. In Chart 3 the seasonal incidence of twin births is shown. We have no explanation as to why there are three times as many births of twins during the month of August as in any other month of the year.

The relation of birth weight to neonatal deaths, as shown in Table II, has been explained on numerous occasions in various reports. In this group studied there were 579 premature babies, for 74 of which the birth weight was not stated; 277 of

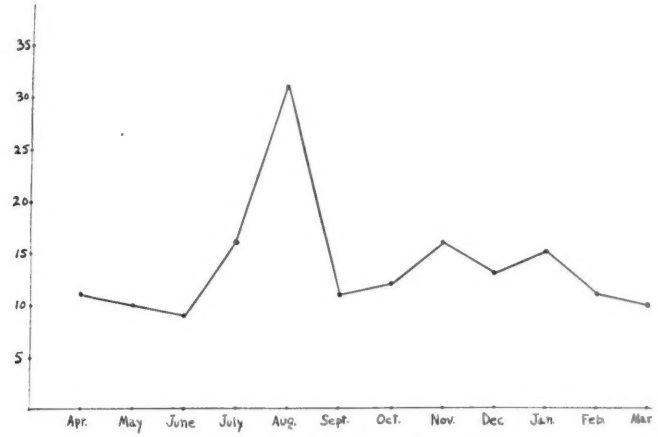

Chart 3.—Seasonal incidence of twin births.

Chart 4.—Seasonal incidence of premature deaths.

these babies weighed less than 3 pounds, and all of them weighed less than 5 pounds. The mortality of prematures varies inversely with the weight, that is, as the weight decreases the mortality increases. There does not seem to be any relation between premature deaths and seasonal incidence of infections. Chart 4 shows graphically the number of premature deaths occurring in the various months of the year. Most of the prematures who die did so in the first twenty-four hours, before infection would have much chance to get started.

The relation of the hours of labor to mortality could be definitely established in 802 of our cases (Table III). In the rest of the group, either because of their being emergencies or too indefinite, the hours of labor could not be determined. It is interesting to note that in 560 of the cases the hours of labor exceeded six hours. In 112 of them it was over twenty-four hours. Because of the difficulty of differentiating between the first and second stages of labor in so many of the cases, this detail was omitted in all.

TABLE III. HOURS OF LABOR

Up to 3 hr.	86	
3 to 6 hr.	156	
6 to 12 hr.	228	560
12 to 24 hr.	220	
Over 24 hr.	112	
Total	802	

The relationship of the types of deliveries and mortality resulting therefrom is shown in Table IV. The lowest mortality rate occurred in forceps when applied to the vertex. Deliveries by this method made up 50.4 per cent of the total, while it only accounted for a mortality rate of 2.3 per cent in that group. The 185 deaths in this type of delivery made up 19.6 per cent of all the deaths. Mid, low, and outlet forceps were the obstetric procedures. There were 5,830 spontaneous vertex deliveries, making up 37.6 per cent of the total deliveries. In this group there were 440 deaths, yielding a mortality of 7.5 per cent, while the 440 deaths accounted for 46.6 per cent of all the deaths. In searching for an explanation as to why the mortality rate in spontaneous vertex is almost three times that of forceps applied to the vertex deliveries, it is noted that there were 251 in the spontaneous group

TABLE IV. TYPES OF DELIVERY

	TOTAL	PER CENT OF TOTAL	DEATHS	MORTALITY PER CENT	PER CENT OF DEATHS
Spont. vertex	5,830	37.6	440	7.5	46.6
Forceps vertex	7,814	50.4	185	2.3	19.6
Versions	532	3.4	78	14.6	8.2
Breech	501	3.2	149	29.7	15.7
Sections	830	5.3	92	10.8	9.7
	15,507				

whose birth weights were under 4 pounds, while in the forceps group there were only 24 babies who weighed less than 4 pounds. In other words, it was not so much the method of delivery as it was the size and development of the child that gave us such a discrepancy in the mortality of these two methods of delivery. If the 251 babies weighing less than 4 pounds are eliminated from the spontaneous deliveries and the 24 similar babies eliminated from the forceps deliveries, the relative percentages are 3.2 and 2. The third lowest mortality rate, 10.8 per cent, occurred in the 830 deliveries by cesarean section. The fourth occurred in versions in which the mortality was 14.6 per cent. The highest mortality rate occurred in the 501 breech deliveries. Although this type of delivery made up only 3.2 per cent of the total deliveries, the mortality rate was 29.7 per cent.

The length of life of the 483 babies who died is analyzed in Table V. It is noted that 216, or 44.7 per cent, lived less than six hours. A fair number of cases did not make any attempt at respirations, but because their heart was beating when de-

TABLE V. LENGTH OF LIFE

Less than 6 hr.	216—44.7 per cent	65.5 per cent
6 to 12 hr.	49—10.2 per cent	
12 to 24 hr.	51—10.6 per cent	
Over 24 hr.	167—34.5 per cent	
Total	483—100 per cent	

livered, were classified as neonatal deaths and helped to increase the mortality in this group. Of the 483 neonatal deaths, 65.5 per cent lived less than twenty-four hours. Most of these babies who died in the first twenty-four hours were among

the very small premature babies. It is this group that is so often spoken of as belonging to the general debility class. This is a very inclusive term and does not help for accuracy. Many believe such a diagnosis can be supported, although our efforts have been to assign a more definite reason for the deaths of these infants, if it is at all possible. It is probably in this group that we see the results of abnormal biochemical relationships and anatomic and physiologic inadequacies in the infant. The problem seems to be to enable the infant to remain longer in the uterus until its physiologic processes are able to function after separation from the mother.

CAUSES OF DEATH

In attempting to outline the causes of death (Table VI) in this group of babies, it was found that there was a great deal of overlapping; that is, two or three conditions could readily exist in the same case, as for example, a syphilitic mother might develop toxemia and give birth to a premature infant. To make a differential classification is not an easy task. Again, it was found in looking over the records of the mothers that certain conditions of health in the mother, other than syphilis and toxemia, might have had decided influence in determining the condition of the child when born. The diseases in the mother that could have had some influence were 8 cases of pneumonia, 15 cases of rheumatic heart disease, 5 cases of diabetes, 2 of tuberculosis, 14 of pyelitis, 18 cases in which an injury or a fall occurred, 3 cases of severe secondary anemia, 8 cases of acute bronchitis, 4 cases of myoma of the uterus, 1 case of severe asthma, and 1 of encephalitis. Again, the causes of death were somewhat influenced by 75 emergency cases. These were women who were not known to the hospital, had had no prenatal care, and either had attempts at delivery at home or perchance the child was born en route to the hospital or was delivered shortly after arrival. Undoubtedly many of these cases were severe and often complicated. So far as possible, however, the cause of death is listed according to the main factor. Again, it seemed important that we should separate the stillbirths from the neonatal deaths, remembering that 48 per cent of our total mortality were stillbirths and 52 per cent were neonatal deaths.

TABLE VI

CAUSE OF DEATH	STILLBIRTHS		NEONATAL DEATHS		TOTAL		350 CASES WITHOUT AUTOPSY	
	CASES	%	CASES	%	CASES	%	CASES	%
Prematurity	121	26.2	157	34.0	278	30.1	113	32.2
Asphyxia	86	18.6	55	11.9	141	15.2	43	12.2
Syphilis	70	15.0	35	7.5	105	11.2	33	9.4
Trauma	46	9.9	66	10.4	112	10.1	17	4.8
Toxemia	53	11.4	25	5.4	78	8.4	33	9.4
Infections	--	---	50	10.8	50	5.2	13	3.7
Malformations	29	6.2	41	8.4	70	7.5	19	5.4
Hemorrhage	3	0.6	26	5.6	29	3.1	4	1.1
Unknown	55	11.9	24	5.0	79	8.4	65	18.5
Other diseases in mother							10	2.8

PREMATURITY

Prematurity undoubtedly is the main factor in causing such a high neonatal mortality, and as was to be expected heads the list as the cause of death in the group studied. In the 579 premature infants it was possible to find a definite cause of death in 301 cases. In the remaining 278 the cause was given as prematurity alone. There were 121 babies or 26.2 per cent of the stillbirths, and 157 or 34 per cent of the neonatal deaths that were thought to be due to this cause. When the 350 cases that did not have autopsy were considered, it was found that 32.2 per cent of this group were stated as due to prematurity. It was not always possible to de-

termine the cause of prematurity. It was noted, however, that there was a relationship between premature births and injury to the mother, sexual intercourse, toxemia, syphilis, displacements of the cord, and placental conditions. It appeared, however, that a fair percentage of the babies were viable and if complications in the mother had not existed it might have been possible for the babies to have survived.

ASPHYXIA

The second highest percentage of deaths occurred in the asphyxial group. This includes those in which there were cord displacements, premature separation of the placenta, placenta previa, and a certain number in which autopsy showed definite evidence of asphyxia without the exact cause of the asphyxia being shown. A good many of these patients were treated by emergency procedures because of the nature of the circumstances. There were 86 or 18.6 per cent in the stillbirth group, and 55 or 11.9 per cent of the neonatal deaths, due to asphyxia; these 141 babies, or 15.2 per cent, died of asphyxial conditions. In the group of 350 cases without autopsy, asphyxia was thought to have been the cause in 12.2 per cent of the cases. It is pretty difficult for us to estimate the influence of anesthesia and analgesics as the cause of asphyxia in the newborn. These procedures are so common in obstetric practice at the present time and successful in many cases, that it is difficult to decide just how much influence they might have had in causing some of these deaths from asphyxia.

SYPHILIS

In the stillbirth group, 70, or 15 per cent, of the deaths were caused by syphilis, while 35 or 7.5 per cent of the neonatal deaths were ascribed to this influence. These 105 babies, or 11.2 per cent, were found to have died from syphilis. This represents the third largest percentage. In this group syphilis seemed to have more of an influence in causing stillbirths than in causing neonatal deaths. Apparently some of the mothers had adequate prenatal treatment. In a good many of them no treatment was given. In a few of the cases with adequate treatment, spirochetes were found in the liver at autopsy. It has frequently been noted how few babies are born in whom signs of syphilis are present during the neonatal period.

TRAUMA

In ascribing deaths due to trauma it seems reasonable to include those in which intracranial hemorrhage occurred together with others in which it might possibly have occurred, but the other injuries, such as fracture or dislocation of vertebrae, decapitation and craniotomy were so important that they seemed to overshadow the intracranial hemorrhage. Just how much hemorrhage into the cranial cavity is necessary to cause death has never been definitely determined. Some blood found in the cranial cavity might very readily be due to autopsy procedures. Undoubtedly the relationship between hemorrhage and anoxemia and other pressure symptoms has a great bearing on the subject. Again it is entirely possible that some of these cases in this group might have survived the intracranial injury if it had not been connected with some other condition such as toxemia, prematurity, and syphilis. Our findings in the study of this group concur with those of others who state that obstetric operations and complications do not cause all deaths from trauma. Trauma may occur under what is considered perfectly normal types of births. There were 46, or 9.9 per cent, stillbirths due to trauma; 40 of them were definitely diagnosed as having intracranial hemorrhage. Sixty-six or 10.4 per cent of the neonatal deaths were caused by trauma; 60 of these were the result of intracranial hemorrhage. One hundred and twelve babies of the group, or 10.1 per cent, died of trauma. When the 350 cases without autopsy were considered, only 4.8 per cent of this group were ascribed to intracranial hemorrhage. This bears out the need for autopsies in arriving at a more definite cause of death. Lumbar or cisternal puncture immediately after death in which blood spinal fluid is secured might be of some assistance in those cases that do not come to autopsy. X-ray of the head and vertebrae of the dead infant might also be of some value in arriving at definite conclusions in this group of cases, especially the ones that do not come to autopsy.

TOXEMIA

The influence of toxemia in the mother on the fetus is well known. Efforts are made either to control the condition or to deliver the baby as rapidly as possible in the severe cases. In this group there were 53 babies, or 11.4 per cent, of the stillbirths who died mainly because of toxemia in the mother; 25, or 5.4 per cent, of the neonatal deaths were in this group, or deaths of 78 babies (8.4 per cent) of the total mortality were ascribed to toxemia in the mother. In the 350 cases without autopsy, 9.4 per cent were ascribed to toxemia in the mother. In most of these cases in this group the primary cause of death was maternal; the secondary or fetal cause was in most cases one of prematurity.

MALFORMATIONS

Thirty years ago malformations caused about the same number of deaths as we find in this report. It can safely be said that there is a strong hereditary tendency in the development of malformations. Just what place the biochemical reactions of the mother have in causing malformations is unknown. There were 29 cases, or 6.2 per cent, of the stillbirths who died because of malformations; 41, or 8.4 per cent, of the neonatal deaths were ascribed to this cause. These 70 cases, or 7.5 per cent, of the total group were thought to have died from malformations. The malformations were usually multiple. They involved the nervous system, the heart, the intestines, the kidneys, either alone or in conjunction with some other condition. In most cases the malformations were inconsistent with life. Of the 350 cases without autopsy, 5.4 per cent of the deaths were ascribed to malformations.

ACUTE INFECTIONS

So far as could be determined, acute infections other than syphilis did not cause the death of any in the stillbirth group. There were 50, or 10.8 per cent, of the neonatal deaths that were due to infection, but when considered with the total deaths, infection was the cause of death in 5.2 per cent. Thirty-six of the infections, or 3.8 per cent, were due to pneumonia of one kind or another. It is our opinion that perhaps most of the infections that occur in the newborn, when sufficiently severe to cause death, are pretty well generalized and probably belong to the septic group. Careful bacteriologic studies before death and at autopsy will show even higher rates for infections. Of the 350 cases without autopsy, 3.7 per cent of the deaths were ascribed to infections. It is noted at autopsy that in nearly all of the cases of massive atelectasis, the lungs of these babies have a certain amount of inflammatory changes on microscopic examination, and are probably after all pneumonias. One case of peritonitis was due to a ruptured gastric ulcer. Two apparently were associated with congenital syphilis; 1 followed a profuse vaginal discharge which at autopsy showed severe pelvic inflammatory disease. Several of the cases of peritonitis followed attempts at reconstruction of malformations of the intestines. Practically all the cases of meningitis were associated with spina bifida, or with surgical attempts to correct the same. There was one case of meningitis which was due to the colon bacillus that was diagnosed several days before death.

Hemorrhage and hemorrhagic conditions are more frequent in the neonatal deaths than in the stillbirth group. Hemorrhage into the lungs, from rupture of the liver, and hemorrhage into the adrenal, are considered in this group although they might conceivably be placed in deaths due to trauma. There were 3, or 0.6 per cent, of the stillbirths that could be ascribed to hemorrhagic conditions, while there were 26, or 5.6 per cent, of the neonatal deaths that were due to hemorrhagic conditions. Sixteen babies died because of hemorrhage into the lungs, from the liver or adrenal, without any other definite evidence of hemorrhagic disease being present. Hemorrhagic disease itself was diagnosed only eight times, erythroblastosis twice, hydrops foetalis three times. Just what hemorrhagic disease of the newborn is has not yet been definitely established. During the past year such a diagnosis

was made in one child, who five months later had developed what appeared to be a typical case of aplastic anemia. Another so-called hemorrhagic disease of the newborn, at two years of age was a typical hemophiliac. Perhaps it would be well to place this group among the malformations, because it may represent a form of malformation of the blood forming organs. In the 350 cases without autopsy, hemorrhage and hemorrhagic conditions were the cause of 1.1 per cent of the deaths.

UNKNOWN CAUSES

There were 55, or 11.9 per cent, of the stillbirths in which no cause of death could be found. There were 24, or 5 per cent, of the neonatal deaths in which no cause of death could be found; that is, 79 of the total, or 8.4 per cent, belong

TABLE VII. PRIVATE CASE RECORD—SEVEN YEARS

Total cases	4,062
Deaths	98
Mortality per cent	2.4
Corrected mortality	40
Corrected mortality per cent	0.98
Autopsies	30

to the unknown group. It is difficult to decide whether a patient has died because of general debility, including prematurity, and should be placed in that group, or whether because of the term and weight of the child and other conditions incompatible with life, it should be put in the unknown group. It is purely a matter of personal opinion. Most of the cases in this group (65) did not have autopsies, and there was insufficient clinical evidence to be sure of the diagnosis. Of the 350 cases without autopsy 18.5 per cent belong in the unknown group.

MISCELLANEOUS

There was one child who died quite suddenly whose mother was diabetic. Perhaps this child died of hypoglycemia but the death was so sudden that correct laboratory tests could not be made and autopsy was refused. There were 18 babies in this miscellaneous group in which the cause of death was doubtful, but they are put in the unknown group or in one of the other general groups. It does not seem wise to have a miscellaneous group of causes of death; for example, there were 5 cases in which an enlarged thymus was found at autopsy and was ascribed as the cause of death. It is doubtful if this can ever be given as a definite cause of death. In 4 other cases there was some placental abnormality which might easily have been the cause of death. These 4 cases were put in the asphyxial group. Seven deaths in the miscellaneous group were caused by direct attempts at self-induced abortions.

COMMENT

Evidently the problem is a prenatal and natal one, and primarily must be solved by the obstetrician. However, there should be very close cooperation between the obstetric and pediatric staffs of all maternity hospitals. It has been our custom at the Philadelphia Lying-in Hospital to make the Pediatric Department responsible for the child as soon as it is born. In all difficult deliveries or other cases where the life of the baby is at stake, the pediatric resident is in attendance. In Philadelphia a general effort is being made through the committees on Maternal Mortality, Stillbirths, and Neonatal Deaths, to get as true a picture of the situation for the entire city as is possible. The committees are advocating adequate prenatal care, careful and complete clinical records, and

detailed autopsies on all deaths. It is hoped also that all the hospitals will institute discussions of their infant deaths before the pediatric and obstetric staffs.

Owing to the very nature of pregnancy, many difficulties are encountered in attempting to find a solution. The problem is a very complex one and will require intensive study. Hereditary influence, the lethal effects of toxins in the mother's blood, her own general health and age during pregnancy, together with her diet and nutrition, undoubtedly have definite effects on the growing fetus. The rate of growth of the fetus, especially during the first two months of pregnancy, is so rapid that cell division and differentiation of tissue constitute an immense hazard. It is no wonder that physiologic inadequacies do occur. The wonder is that they do not occur more often than we have been able to demonstrate. As most of the stillbirths and neonatal deaths are associated with prematurity, one cannot help wondering whether Mother Nature is allowing the spotted and stunted fruit to fall and perish early. However, after seeing numerous small premature infants grow and develop normally one cannot allow such an idea to enter into this problem of neonatal mortality. Many of the problems of this age period are undoubtedly on the borderline between physiology and pathology, and this will require careful biochemical studies to indicate the proper solution. Imperfect physiologic function plays a part, and perhaps a bigger part than we can conceive of at present.

Mortality rates vary considerably in different places, even though there seems to be a great similarity in nursery routine, method of feeding and general equipment. Postnatal care in such instances does not seem to be the answer. Perhaps it is the vitality of the groups in question which in turn is materially affected by maternal conditions, social and economic status, and obstetric procedures. So often our autopsy reports are completed with the statement that the cause of death is unknown. This fact points out the need for well-trained pathologists who will be willing to investigate minutely the structural changes in the organs of the newborn babies. Even this does not seem to offer much information regarding the functional ability of the various organs. Undoubtedly the spread of general health education, and better understanding of congenital syphilis and toxemia and their treatment, preventing accidents at birth, the prevention of and improved care of premature infants, will in turn have some influence on neonatal mortality.

SUMMARY AND CONCLUSIONS

1. A study of 944 infant deaths in a seven-year period at the Philadelphia Lying-in Hospital is presented.

2. Close cooperation of the obstetric and pediatric staffs is advisable.

3. Infant deaths should be reviewed at the monthly staff meetings. Errors in judgment and technique should be pointed out and responsibility fixed.

4. Skilled pathologists should perform the autopsies. Microscopic sections should be made and postmortem cultures taken.

255 South Seventeenth Street

RETROPERITONEAL CYSTIC LYMPHANGIOMA

CLARENCE B. INGRAHAM, M.D., AND JOHN M. NELSON, M.D.,
DENVER, COLO.

(From the Departments of Obstetrics and Gynecology and Pathology of the University of Colorado School of Medicine and Hospitals)

IT HAS been our opportunity to study a case of retroperitoneal lymphangioma which we report because of its rarity and unusual size. This case, together with four collected from the literature by Kretschmer and Hibbs[1] to which they added one of their own and a case described by Sick,[2] bring the total number of such lymphangiomas to seven.

HISTORY OF CASE

Mrs. B., aged 32, entered the Colorado General Hospital on Feb. 26, 1935. Approximately four years previously she had noticed a growth in the abdomen which she described as being as large as the clenched fist. Six months later she was operated upon in one of the smaller Colorado towns. At this time the tumor was said to be as large as a football, and was believed to be a "carcinoma involving the large bowel, and inoperable." A small piece examined by a pathologist was reported as being benign. Following the operation the patient experienced a coughing seizure, the incision opened and a considerable discharge followed. Upon leaving the hospital she states that the tumor gradually increased in size to December, 1934, when she was given intravenous colloid gold. After which, growth was rapid, and though she thought she was losing flesh, she actually gained 14 pounds. She continued doing her housework, but with difficulty because of heaviness and the size of the abdomen. She was short of breath but experienced no actual pain. There was no swelling of the ankles.

About one week before presenting herself to us she began to have almost constant nausea; there was a slight elevation of temperature, with a feeling of malaise; the bowel and urinary functions were normal.

The patient's menstrual history was normal, she had had five children and one induced abortion. There was nothing else of importance in her history.

Physical Examination.—On admission there was a slight cough, and a fever varying from 100 to 102° F.; the pulse was 100 to 120.

The abdomen contained a large, firm, cystic-feeling tumor, nodular along its inferior margin, smooth over the anterior and upper surfaces. This projected over the symphysis pubis and extended above to the ensiform (Fig. 1). There was tympany in both flanks.

On pelvic examination the tumor could be felt at the brim of the pelvis, with a small uterus distinct from the growth above.

The urine was normal, the blood pressure 120/80. The red blood cell count was 3,520,000 with hemoglobin 11.5 gm. The leucocytes were 14,000 with 85 per cent polymorphonuclear leucocytes.

Operative Findings.—On opening the abdomen from the symphysis to 3 inches above the umbilicus, the tumor was seen to be retroperitoneal (Fig. 2). The transverse colon ran across the upper part of the growth and the small intestines were pushed to the sides and lay in the flanks. The posterior parietal peritoneum over the tumor was adherent to the peritoneum of the anterior abdominal wall in the right upper quadrant. These adhesions were fairly firm and were freed. The posterior parietal peritoneum over the tumor was opened in the midline, clamping the large vessels which ran in the retroperitoneal layer and communicated in places with those within the capsule of the tumor.

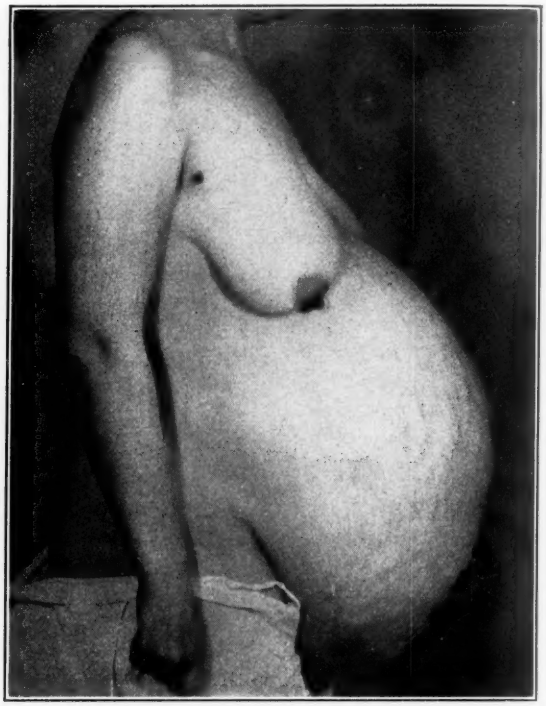

Fig. 1.—Patient prior to operation.

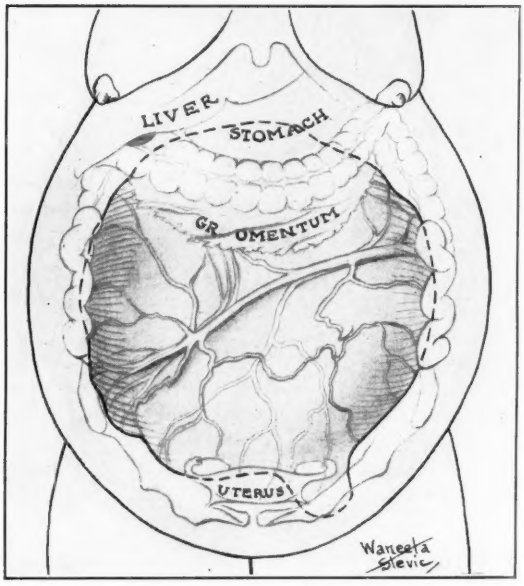

Fig. 2.—Retroperitoneal cystic lymphangioma. Schematic representation of position of tumor with anterior abdominal wall removed. Shaded area and dotted line indicate tumor.

The tumor was quite easily shelled out by blunt dissection with the hand. In the lower left portion of the abdominal cavity the projection shown in the photograph (Fig. 3) lay under the upper portion of the sigmoid and left broad ligament and extended to the abdominal opening of the inguinal canal. There was some bleeding in a few areas, but this practically ceased on removal of

Fig. 3.—Gross specimen, anterior surface, showing projection which extended to the left internal inguinal ring.

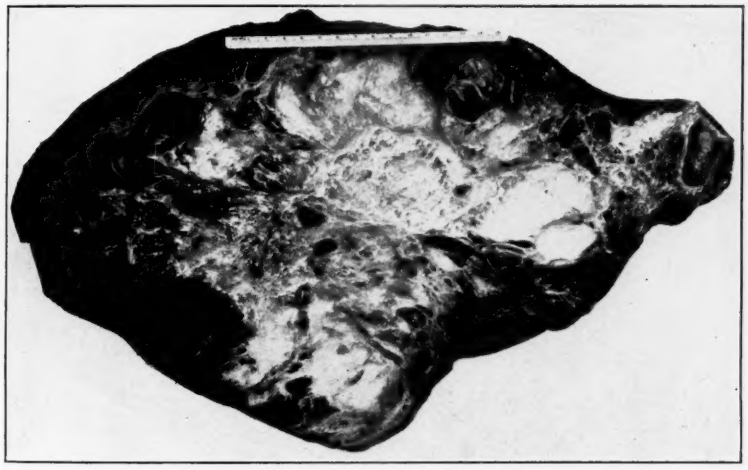

Fig. 4.—Cut surface of tumor after fixation.

the tumor. The peritoneum was sewn over, tying off the large vessels. The retroperitoneal cavity remained dry. The gall bladder, kidneys, uterus, tubes, and ovaries were grossly normal. The patient ran a temperature of 101° to 104° F. for five days with a pulse of 110 to 120. This subsided and was attributed to absorption from the large retroperitoneal space. The convalescence was subsequently normal and the patient left the hospital apparently well.

One year after operation the patient was in good health with no apparent recurrence of the tumor.

Gross Description.—The specimen was an elliptical-shaped mass of tissue with a rounded projection extending from the lower border. The mass measured 46 by 43 by 21 cm. (18 by 17 by 9 inches) and weighed 18 kilograms (40 pounds). The external surface was bluish red in color and smooth for the most part although there

Fig. 5.—Photomicrograph of section of retroperitoneal lymphangioma showing large spaces (low power).

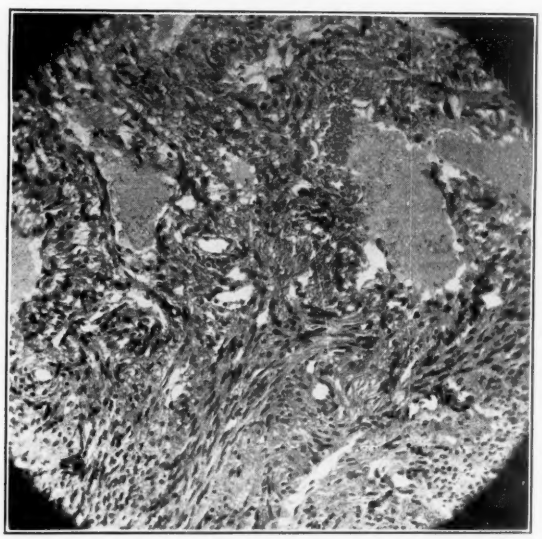

Fig. 6.—Photomicrograph of section of tumor showing smooth muscle fibers (high power).

were adherent tags of connective tissue. From the surface projected a number of low rounded lobulations measuring from 8 to 2 cm. in diameter (Fig. 3). Beneath the surface were numerous blood vessels, some of which measured 0.5 cm. in diameter. These stood out like blue cords. The mass had a semisolid consistency and was apparently cystic in structure.

The specimen was opened by a longitudinal incision along its greatest diameter. When sectioned, a serous blood-tinged fluid poured forth from numerous cystic cavities. None of this fluid was mucinous or coagulated. The cystic spaces ranged in size from 8 cm. down to microscopic dimensions, the majority being 0.5 to 1.0 cm. in diameter (Fig. 4). They had smooth gray glistening walls and some of them communicated with one another while others appeared as solitary spaces. The spaces, for the most part were located on the periphery of the mass, giving it a honeycombed appearance while the center was occupied by a more solid mass of tissue, the cut surface of which was purplish white with gray trabeculations. A comparatively small number of cystic spaces were seen in the central area.

Microscopic Examination.—The tumor consisted of numerous spaces of all conceivable sizes and shapes. These spaces contained a finely granular eosin-staining precipitate. A few spaces contained red blood cells, all of which gravitated to one side of the spaces (Fig. 5). The lining of each space was a layer of flattened endothelial cells with small oval and spindle-shaped granular nuclei. The wall between some of the larger spaces was composed of a very thin layer of fibrous connective tissue. Other spaces were separated by a thick layer of edematous fibrous connective tissue which contained bundles of smooth muscle fibers and collections of lymphocytes (Fig. 6). The blood vessels were not numerous. They were congested, dilated, and had poorly developed muscular walls. The more solid mass of the tumor was composed of bundles of fibrous connective tissue and smooth muscle which resembled uterine muscle in structure and arrangement. There was some hyalinization of the fibrous connective tissue throughout these areas as well as slight lymphocytic infiltration and edema.

Pathologic Diagnosis.—Retroperitoneal cystic lymphangioma.

REVIEW OF THE LITERATURE

Kretschmer and Hibbs[1] in 1934 reviewed the literature on retroperitoneal lymphangiomas and summarized the previous cases. They included four cases to which they added one of their own. That the extreme rarity of this condition might be questioned was mentioned by these authors and also McFadden.[3] Retroperitoneal cysts, thought to have been derived from the urogenital ridge or from misplaced peritoneal cells are described more frequently. Warfield,[4] discussing mesenteric and retroperitoneal cysts of various types, estimated that 400 such cysts have been reported. McFadden,[3] who reported a retroperitoneal lymphangioma, said, "Looking over the published papers and the description of cases, this case suggests that retroperitoneal cysts are true lymphangiomas and not cysts arising from local peritoneal cells or from cells derived from the urogenital ridge."

Makins[5] is also of the opinion that most mesenteric and retroperitoneal cysts are lymphangiomas. Ewing[6] devoted a paragraph to retroperitoneal lymphangioma and made no mention of the rarity of the condition.

On the other hand, Sick[2] described a case of multiple retroperitoneal lymphangioma and made no mention of any previous cases. Gaudier and Gorse[7] (quoting Kretschmer and Hibbs[1]) reported a retroperitoneal cystic lymphangioma and drew attention to the fact that diligent search of the literature revealed no strictly analogous case. Westman[8] reported a retrocecal lymphangioma and Burhaneddin[9] a multilocular cystic retroperitoneal lymphangioma. Both of these authors could find no similar cases in the literature.

Reviewing all types of retroperitoneal tumors Magoun,[10] Andrews,[11] and Schmid[12] did not include any cases of retroperitoneal lymphangiomas. Schmid,[12] who collected 297 cases of retroperitoneal tumors, stated that, "Cysts of varied types are rarely seen."

Until the nature of mesenteric and retroperitoneal cysts, thought to be derived from the urogenital ridge and peritoneal cells, is determined, we prefer to believe that retroperitoneal lymphangiomas are rare, and add our case to the six previously described.

Pathology.—Kaufmann[13] described lymphangiomas as variously shaped, diffuse or circumscribed neoplasms, the chief constituents of which are spaces lined with

endothelium and containing lymph. These spaces in some cases are enormously distended and in others the walls are remarkably thickened. For purposes of classification the original description of lymphangiomas by Wegner was followed by Kaufmann.[13] Wegner divided lymphangiomas into (a) simple lymphangiomas, usually situated superficially in the skin, (b) cavernous lymphangiomas, found chiefly in macroglossia, macrocheilia, and more rarely in other parts of the face and skin, (c) cystic lymphangiomas, consisting of cysts, simple or subdivided, lined with endothelium, the contents of which are clear, serous, milky, or chocolate-colored fluids which may contain cholesterin and detritus. These tumors appear chiefly in the neck, breast, axilla, lower sacral region, abdomen, thighs, and inguinal regions. When located in the mesentery they often contain chyle, in which case they are called chylangiomas.

The majority of authors are inclined to believe that these tumors arise from misplaced embryonal lymphatic tissue. Ewing[6] believed they are probably of embryogenic origin. Thompson and Keiller,[14] discussing the etiology of lymphangioma of the neck, traced the embryologic development of the lymphatic system and believed these tumors arise from embryonic rests, the sites of predilection being the neck and the region of the iliac vessels because the anlage of the lymphatic system appears in these areas.

One other factor believed to be important in the development of these tumors is passive dilatation with hyperplasia of the pre-existing lymph vessels (lymphangiectasis). Schmid[12] quoting Kaufmann[13] thought that lymph stasis plays an important part, leading finally to muscle hypertrophy and tumor formation. Ewing,[6] however, was able to demonstrate free communication between afferent and efferent vessels in several lymphangiomas and concluded that stasis could not have been present in these cases. Kretschmer and Hibbs[1] mentioned the fact that lymphangiomas, which are true neoplasms, and lymphangiectasis are separated from one another with difficulty at times and emphasized that a sharp differentiation should be made between the two conditions.

Concerning the enlargement of lymphangiomas, proliferating buds of endothelium forming new lymph vessels have been fully recognized in certain cases (Ewing[6] and Kretschmer and Hibbs[1]). That this is not entirely the case has also been brought out by Ewing[6] who stated that in some of the largest cystic lymphangiomas the signs of neoplasm are the least distinct. Thompson and Keiller[14] postulated that the endothelium under certain conditions may secrete fluid and that due to some alteration in the permeability of the vessel wall little of the fluid is reabsorbed with resultant cyst formation and tumor enlargement. In Sick's[2] case, one of the retroperitoneal cysts was marsupialized, and at various times during the day there was a marked increase in the amount of watery secretion.

The pathologic reports of the previous cases of retroperitoneal lymphangioma, except that of Sick,[2] have been adequately summarized by Kretschmer and Hibbs.[1] Sick's[2] case is significant enough to be reported more fully in this paper. At autopsy two large cysts were encountered on examination of the peritoneal cavity. The largest was located in the left upper quadrant near the jejunoduodenal juncture. A small spherical cyst, measuring 8 cm. across, was located on the right side below the kidney and above the brim of the pelvis. When the small intestines were removed, a cushionlike mass of retroperitoneal cystic spaces with a nodular firm consistency was encountered. It partially covered the pancreas and kidneys and extended down to the promontory of the sacrum. The ascending colon was pushed forward and to the side, the mesenteric attachment of the small intestines up and towards the liver. This mass was most marked on the right side of the abdomen and gradually blended with normal retroperitoneal tissue on the left.

Microscopically the tumor consisted of slitlike spaces lined with characteristic endothelium. The stroma of the larger spaces had bundles of smooth muscle which in instances formed an almost continuous wall about the space. In the connective tissue there was infiltration with plasma cells, lymphocytes, and mast cells. Many of the spaces contained cholesterin.

Retroperitoneal lymphangiomas vary markedly in size and shape. The largest heretofore reported was Burhaneddin's[9] case. This tumor measured 45 by 30 cm. (18 by 14 inches), and weighed 6.4 kilograms (14 pounds). The smallest tumor, Westman's[8] case, was the size of a clenched fist.

Of the seven retroperitoneal lymphangiomas (including ours), four were located on the right side of the spinal column. Sick's[2] case was predominantly right sided. The remaining two occupied the space on both sides of the spine. Three of the tumors had fingerlike projections to or into the inguinal rings. Two were located on the right and one on the left side.

All of the lymphangiomas were cystic in nature, the size of the cysts varying from 8 cm. to microscopic dimensions. The fluid in the cystic spaces, mentioned in three cases, was chocolate colored in two, clear in one. Cholesterin was mentioned in Sick's[2] case, and after fixation, a gelatin-like substance containing homogenous opaque yellow-brown material in its center was noted by Kretschmer and Hibbs.[1]

Microscopically evidence of malignancy was found only once in the series. Kretschmer and Hibbs[1] found the endothelial lining of many of the cysts to be hyperplastic in nature. No mitotic figures were seen.

The stroma of these tumors was found to contain smooth muscle in 3 cases, Sick's,[2] McFadden's[3] and ours. The stroma of Kretschmer and Hibbs[1] case was made up of fibrous connective tissue undergoing atrophy and hyalin degeneration. Lymphoid tissue having a lymph node arrangement was observed by McFadden.[3] Several collections of lymphocytes were found in our case. Kaufmann[13] mentioned that the fibrous connective tissue stroma may partake in the neoplastic growth of true lymphangiomas and at times may overshadow the endothelial proliferation, in which case it is proper to call the tumor a lymphangiofibroma. The tumor in our case showed a predominance of smooth muscle in many areas and might justifiably be classed as a retroperitoneal lymphangioliomyoma.

DISCUSSION

While cystic lymphangioma is fairly common, the occurrence of these tumors in the retroperitoneal space is, to the extent of our knowledge, rare. There is some confusion in the literature as to the pathologic nature of retroperitoneal cysts. We feel that this phase of the subject should be clarified. The cases referred to and reported in this paper are all cystic lymphangiomas and may be of some help in the subsequent classification of these tumors.

SUMMARY

A case of retroperitoneal lymphangioma is reported in detail. Five cases have been summarized by Kretschmer and Hibbs.[1] To this number we have added a case described by Sick,[2] bringing with our own, the total number of such cases to seven. To our knowledge there is nothing characteristic about such tumors whereby they may be diagnosed prior to operation. Of the seven cases reported, five patients have survived operation successfully.

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POST-PARTUM HEMORRHAGE AS A CAUSE OF DEATH*

CLAYTON T. BEECHAM, B.S., M.D., PHILADELPHIA, PA.

THE purpose of this study is to analyze the etiology and details of various methods of treatment as shown by the records of 52 deaths from post-partum hemorrhage in the 183,384 deliveries in Philadelphia, over a six-year period, 1931 through 1936. Post-partum hemorrhage was the direct cause of death in 52 cases, 0.028 per cent, or once in every 3,527 labors. These figures are similar to those quoted by Williams,[1] "Fatal hemorrhage is fortunately rare, having occurred in 0.03 per cent or once in 3,121 times." The Maternal Welfare Committee of the Philadelphia County Medical Society judged 32, 61.5 per cent, of these deaths as preventable. The responsibility for 28 deaths, 53 per cent, was assigned to the attendant, as treatment in all was deficient. Four of the fatalities, 7.5 per cent, were due to ignorance of the patients; while 20, 38 per cent, were termed nonpreventable. All else passes into insignificance before the fact that the Committee felt over one-half of the deaths were preventable.

Forty-one patients in this series, 79 per cent, were delivered in hospitals, while 4, 7.6 per cent, of those delivered at home were taken to the hospital after the complication developed. Three of the patients were attended by midwives who called in physicians when the post-partum hemorrhage occurred. Medical students were in attendance on 3 cases, 2 of which were hospitalized and the third lived eight hours while the student tried to get some one to come to his aid.

The incidence of spontaneous deliveries in this series of post-partum hemorrhage cases is 42.3 per cent, contrasted with an average of 72 per cent in all births, as shown by the first "three-year study" in Philadelphia. The incidence of version, 15.4 per cent, in this series is ten times as high as the average incidence of version in the hospital deliveries of the City in the first three years of this study, 1.52 per cent. Indications for the operative interference were not made clear, and two history charts carried the notation of "elective version."

In our consideration of treatment in these cases it is well that we know the interval of time between delivery and death of the mother. Is there time for adequate treatment once this accident has occurred? Here we find our most variable figures, since death came anywhere from one and a half hours up to seventeen days following delivery. To arrive at a time interval, we excluded 4 cases from the average, since this accident, for the most part, shortly follows labor and not several days later. These 4 cases will be considered separately as late post-partum hemorrhage.

The usual story was not that of sharp, marked hemorrhage for a few minutes and then sudden death. Rather the picture brought to light by this study was one of steady moderate bleeding over a period of several hours, ending in shock and death because no one became

*Read before the Philadelphia Obstetrical Society, March 3, 1938.

alarmed. There was an occasional case where bleeding was sudden and great in volume, with the patient going into shock rapidly, but even in such a case there was usually time for adequate treatment. Thus we find the average time between delivery and death of the mother, as five hours and twenty minutes. Only 6 patients, 11.5 per cent, died within two hours of delivery and none in less than one and a half hours. In the vast majority of cases there was adequate time for very intensive treatment. A fairly typical case is the following:

This patient was delivered at home by her physician, assisted by a nurse. Labor was easy and uncomplicated. The placenta was not expelled and since there was no alarming hemorrhage, nothing was done except watchful waiting. Bleeding was described as "constant seepage," and four hours after delivery she was admitted to the hospital in shock. General supportive treatment and intravenous saline were administered. No attempt was made to deliver the placenta, since the patient was "not bleeding a great deal." However, she died in shock seven hours and forty minutes after delivery.

The causes of bleeding in this series were variable. In 27 cases hemorrhage was due to either retained placenta (14), abruptio placentae (7), or inertia uteri (6). Fourteen patients were classed as "unexplained," since their histories gave no clue as to the condition of the uterus while bleeding was going on. We might well infer, since no apparent cause was given and the patient continued to bleed, that we were dealing with inertia uteri. This inference might or might not be true, consequently we assigned no cause. Table I gives the etiologic factors involved in the entire series. Toxemias of pregnancy were associated as contributory causes in six deaths. Pre-eclampsia appeared in 3 cases, eclampsia, nephritic toxemia and an ill-defined type (low blood pressure), each once.

TABLE I. ETIOLOGY, PERCENTAGE DISTRIBUTION

Retained placentas	26.9 per cent
Abruptio placentae	13.4 per cent
Inertia	11.5 per cent
Lacerated cervix, lacerated perineum	3.8 per cent
Uterine fibroids	3.8 per cent
Partial placenta previa	3.8 per cent
Purpura hemorrhagica	1.9 per cent
"Lacerated uterus"	1.9 per cent
Retained placentas, lacerated perineum, cervix and uterus	1.9 per cent
Unexplained	26.9 per cent

Methods employed in the treatment of post-partum hemorrhage were often haphazard and lacking in uniformity. Uterine packing was employed in only 28 cases. Notwithstanding the fact that bleeding continued through the packing in most instances, only 12 were repacked. Vaginal packing alone was employed in 3 cases for uterine bleeding. In this respect, let us consider a case report:

To hasten delivery, a physician used two ampoules of pituitary solution. Following the birth of the baby, ergot was given by mouth. The placenta was adherent

so the physician packed the vagina. Six hours later the patient had a severe hemorrhage. The vagina was packed again, the bleeding continued, and she died nine hours and twenty minutes after delivery.

Six of the 14 retained placentas were manually removed and the uteri packed. No reasons were given as to the cause of retention and no mention was made of placenta accreta. Traditional treatment for retained placenta is manual removal, yet 7 died without any attempt at completion of the third stage of labor.

The most common therapeutic measure employed was intravenous fluid. Thirty-six patients, 69.2 per cent, were given parenteral fluid either in the form of physiologic saline or in combination with glucose. Pituitary solution and some form of ergot found use in 48 per cent of all cases. Only 30 per cent of the patients received blood transfusions. This is most regrettable since 79 per cent of the deaths were hospital deliveries. More appalling is the discovery that eight patients, 15.3 per cent, went into shock and death with apparently no attempt at treatment. The following case report is only to illustrate that "it can happen here":

This patient entered the hospital in active labor. The "head was found to be engaged and the cervix four fingers dilated." The membranes were unruptured. Because of "dystocia" three minims of pituitary solution were given, following which, the membranes ruptured. Shortly thereafter, high forceps were applied and the baby was extracted with difficulty. This procedure resulted in a complete perineal tear and "bilateral lacerations of the uterus." A part of the placenta was left in. There was no record of therapy employed or even an attempted repair. The patient was taken from the delivery room in shock and still bleeding profusely. Death occurred two hours and forty minutes after delivery.

Hot intrauterine douches were used without advantage in two cases, while hysterectomy in three proved to be of little help. To illustrate this last named procedure, let us consider the following case:

This patient developed pre-eclampsia and was hospitalized. For two days she received active treatment and improved. Next she was given a medical induction of labor and delivered spontaneously with no difficulty. Ten minutes later the placenta came away spontaneously. Twenty minutes later the patient began to bleed freely and despite adequate doses of oxytocics, the uterus would not contract. She was packed with gauze, but the bleeding continued through the tampon. An intravenous infusion was started while the patient was wheeled to the operating room, where a hysterectomy was done. More intravenous fluids were administered and a 500 c.c. blood transfusion was given. Notwithstanding prompt and efficient treatment, the patient died four hours after delivery.

Late post-partum hemorrhage was fatal to 4 women in this series. All had retained secundines, while one developed puerperal sepsis, but died of hemorrhage on the seventeenth day. Three patients died eight, ten, and twelve days following delivery; only in one instance was an attempt made to evacuate the uterus. Table II presents the various treatment methods used in these cases. In the light of retrospection, let us bear in mind that we do not know how many women with post-partum hemorrhage were successfully treated with the very same procedures employed here with failure.

It is hardly expedient to discuss treatment without having first considered prophylaxis. Prevention of post-partum hemorrhage begins in the prenatal period, with physical conditioning of the patient,

paying particular attention to her nutrition. All foci of infection should be eliminated and any existing anemia treated. A history of a previous post-partum hemorrhage, or where fibroids are present, or any condition causing overdistention of the uterus, should indicate a blood typing for that patient. In short, the pregnant woman should have the benefit of close medical study throughout her prenatal period, so as to give her ideal preparation for delivery. When labor commences, precaution against a developing inertia uteri is most important. Adequate and judicious sedation, nourishment, either oral or parenteral, are measures of paramount importance.

Proper management of the third stage of labor is most important. A procedure of definite prophylactic value is the administration of 1 c.c. of pituitary solution and 1 c.c. of aseptic ergot, as soon as the second stage of labor is completed, thus allowing the placenta to be expelled with little or no massage. We made mention of this[2] as a matter of routine, and Adair did not agree with us stating,[3] "that the routine use of any oxytocics during the third stage of labor is undesirable as it is likely to cause perversion of the normal mechanism." The normal mechanism is for the uterus to be left alone to contract and expel its placenta, but in most clinics it consists in the operator or the nurse massaging the uterus into contraction, expressing a placenta frequently not completely separated. Certainly this must be a traumatic procedure and it logically follows that post-partum hemorrhage might very well develop from such maltreatment. On the other hand, the oxytocics described when employed will contract the uterus with as little damage as possible and keep it contracted. Only rarely is one required to do a forceful expression. Many question this procedure, feeling that oxytocics following the birth of the baby will cause retained placentas. Here again we are able to say that such a complication has not been noted. However, Davis, Adair and Pearl[4] disagree, holding the opposite view that such a course "may eventuate in a post-partum hemorrhage" since it "may cause a contraction zone at the lower uterine segment, resulting in incarceration of a partially or incompletely separated placenta." The results we have seen do not support this contention. We know that the lower uterine segment is passive in its action, and should it contract it would be feeble at best. Schumann has had the above plan in operation for six years at the Kensington Hospital for Women, with a resultant extremely low incidence of even alarming blood loss, and it has proved to be a most helpful prophylactic measure.

In the treatment of post-partum hemorrhage two procedures stand out above all others; early transfusion and packing. At the first sign of abnormal amounts of bleeding, donors should be procured and held in readiness. In face of hemorrhage, thorough search should be made for lacerations in the body of the uterus (particularly after version), the cervix and the vagina, and these should be treated appropriately, either hysterectomy, repair, or packing.

TABLE II. FORMS OF TREATMENT EMPLOYED IN THIS SERIES
PERCENTAGE DISTRIBUTION

Intravenous fluids	69.0 per cent
Oxytocics	48.0 per cent
Placentas manually removed	46.0 per cent
Uterine packing	44.0 per cent
Blood transfusion	30.0 per cent
Repacked	23.0 per cent
Uterovaginal packing	9.6 per cent
Vaginal packing	5.7 per cent
Hysterectomy	5.7 per cent
Hot douches	3.8 per cent
No treatment	15.3 per cent

If the placenta has not already been delivered, it should be manually removed, and the removal followed by intrauterine and vaginal packing. The most satisfactory pack is one completely filling the uterus in a firm manner, following through to the vaginal outlet. Particular attention should be paid to the lateral fornices of the vagina where a well-placed pack will help to cut down the uterine blood supply. Should the bleeding continue through the packing, the uterus and vagina may be repacked, at least where technique was questionable the first time.

Ergonovine either intravenously, hypodermically, or rectally instilled is a valuable aid in contracting a uterus but cannot be relied on to the exclusion of the other steps mentioned.

Until blood donors are available, one of the easiest and most useful measures to be employed is intravenous fluid, either in the form of glucose and saline, gum acacia, saline or Ringer's solution. It found employment in 69 per cent of the cases, and we could see little reason why it was not used in 100 per cent of the patients. The intrinsic value of saline intravenously has long since been proved as an aid in combating hemorrhage and shock.

The difficulties encountered in securing proper donors for emergency transfusions is well known. However, a "blood bank" in every hospital would offset such difficulties. This blood supply may come from the hospital personnel or better, the plan recently proposed by Goodall, Anderson, Altimas and MacPhail. A preliminary report by Goodall and others shows fetal cord blood collected under aseptic conditions to be an "inexhaustible source of blood for transfusion, preserved at a minimum of cost, and preservable in its usefulness as a transfusion medium for at least sixty days." It must be remembered in transfusions for post-partum hemorrhage that blood must be replaced in amounts lost. Beck in his text tells of a patient needing 2,500 c.c. of blood to save life after a post-partum hemorrhage.

Hysterectomy is the most heroic treatment for post-partum hemorrhage. It should be held for the exceedingly small group of cases where everything possible is done and yet the patient continues to bleed. If one were to treat a patient wherein all lacerations had been

sutured, uterus and vagina packed, and repacked, if necessary, transfusion and intravenous fluids had kept the patient in fairly good condition and yet the bleeding persisted, hysterectomy would be the treatment of choice.

COMMENT

In this brief report we would like to call attention again to the judgment of the Maternal Welfare Committee of Philadelphia in terming 53 per cent of such deaths as preventable, with the responsibility assigned to the attendant. We have found the average time between delivery and death of the mother from hemorrhage to be five hours and twenty minutes, yet only one-half were packed and less than one-third had blood transfusions. Very few cases indicated anything but a haphazard plan of treatment. We have outlined accepted steps in the treatment of postpartum hemorrhage, all of which are within the scope of any modern hospital and staff.

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250 South Seventeenth Street

DISCUSSION

DR. THADDEUS MONTGOMERY.—Retention of the placenta is responsible for the largest number of maternal deaths in the series. This requires special attention.

Even in normal spontaneous delivery difficulties with the placental stage constitute a major hazard in the etiology of post-partum hemorrhage, particularly if the attendant is lacking in practical experience. Thus several of the deaths have occurred in spontaneous delivery inaugurated in the home—the attendant having had difficulty in expressing the secundines and his efforts having served perhaps only partially to detach the placenta.

With the wide acceptance of operative delivery, median episiotomy, immediate repair, deep analgesia and anesthesia, the hazards of this complication have been vastly increased. The effects of deep analgesia and of surgical anesthesia for delivery reveal themselves principally in the third stage, and unless the operator is very much on his guard he will very suddenly find himself in difficulty.

Of very great importance is the estimation of the patient's condition at the immediate conclusion of the delivery of the baby. If the condition is not good, it is imperative that further surgery be abandoned for the time, that all reparative work be postponed, and if bleeding is present, the uterus be promptly emptied and packed.

For myself, I much prefer to stop the anesthetic at the conclusion of the second stage and attend solely to the resuscitation and treatment of the baby and the management of the placental delivery. When the placenta is completely delivered, the uterus firmly contracted, and the patient's condition found to be excellent, the repair work, under further anesthesia, may be proceeded with.

This makes of the management of labor two separate steps, the first of which, the delivery, is to be entirely completed (child, placenta, and membranes) before proceeding with the second, the repair. The second step is never undertaken until it is certain that the patient has successfully and safely completed the first.

DR. J. C. HIRST.—I was very much interested in reviewing the statistics reported by Dr. Beecham to note that in these deaths from hemorrhage there were five sets of twins reported, an extremely high proportion. Multiple pregnancy is thus a predisposing factor to hemorrhage.

DR. CARL HENRY DAVIS.—It has been my belief for years that when the uterus is much overdistended, regardless of the cause, there usually is more bleeding post partum.

While Dr. Beecham's discussion of treatment was excellent, no mention was made of the Trendelenburg position for patients who are in shock from the loss of blood. If the patient is placed in this position and given oxygen, it may be possible to prevent damage to the brain during the interval which usually elapses before adequate blood can be secured by means of transfusion.

I do not like to introduce large amounts of fluid into the circulatory system until the bleeding has been stopped by appropriate means. It is probable that some patients have been lost through premature introduction of fluids.

DR. JOHN A. SHARKEY.—Version, and version and craniotomy accounted for 17.3 per cent of 52 deaths. In the first Philadelphia survey, version had a mortality of 6 per cent; in the same survey the cesarean section mortality was 5.5 per cent. In 22 of the version deaths the uterus was ruptured. It would be interesting to know whether or not these versions were done by experienced operators, in order that we may properly decide whether version is slightly more dangerous than cesarean section.

For several years we have been using pituitrin and ergot intramuscularly immediately after the baby is born and agree with Dr. Beecham that it materially reduces the amount of post-partum bleeding. Occasionally we have noted with this technique that the placenta becomes imprisoned in the lower uterine segment or cervix but one has only to wait about fifteen minutes for relaxation to occur. In addition if there is more than what we consider normal bleeding we give ergonovine intravenously and have found it very useful. However, in certain cases all of these measures will fail and packing of the uterus must be done. It is hard to understand why only 44 per cent of these patients were packed since this alone is perhaps the best single remedy we have for the control of post-partum hemorrhage, assuming of course that lacerations of the vagina and cervix have been properly treated. There were 23 per cent of these cases repacked. We feel that, when a uterus has been packed and repacked and still continues to bleed, hysterectomy should be done, leaving the second packing in the uterus until one is ready to open the abdomen. Certainly it would seem that, in patients with placenta previa and abruptio placentae who continue to bleed, hysterectomy should be considered; not, however, until the patient has been given some blood and allowed to recover partially from her shock. She should have more blood transfusions again after the uterus is out.

From Table II one might assume from the number of saline infusions as compared to blood transfusions, that the former were held to be the more valuable, since they were used in 69 per cent of the cases as against 30 per cent for blood transfusions. The exact reverse of this is actually true. We feel that blood transfusions should have been given in 100 per cent of the cases in this series since the average time between delivery and death was five hours and twenty minutes. With the inauguration of "blood banks" in various hospitals, no woman should die of post-partum hemorrhage after hospital delivery in Philadelphia without having been transfused with blood in sufficient amount.

INHIBITING EFFECT OF PENTAVALENT ARSENICALS UPON TRICHOMONAS*

Comparative Efficacy and Toxicity of Acetarsone, Carbarsone and Aldarsone in Laboratory Studies

A. E. Rakoff, M.D., Philadelphia, Pa.

(From the Department of Obstetrics, Jefferson Medical College Hospital)

THE employment of pentavalent arsenicals for the treatment of trichomonad infestations is becoming more prevalent. For freeing laboratory animals from intestinal infestations with trichomonads, carbarsone has been used by Hegner and Eskridge[1] and by Gabaldon,[2] while acetarsone has occasionally been administered to human beings for this purpose.[3]

The three drugs in this group which have been recommended as trichomonadicides are acetarsone (3-acetylamino-4-hydroxy-phenyl-arsonic acid), carbarsone (p-carbamino-phenyl-arsonic acid) and aldarsone (sodium-methylene-sulfon-amino-hydroxy-phenyl-arsonate).[4] Comparative chemotherapeutic studies of the three arsenical preparations have not been reported, although a few clinical and laboratory observations concerning the effect of these preparations upon trichomonads or trichomonad infestations are available. In an earlier study Bland and Rakoff[5] gave comparative results of the killing effect of acetarsone and aldarsone on vaginal trichomonads and their relative efficacy in the treatment of vaginal trichomoniasis.

Several methods have been described for testing the effect of drugs upon trichomonads in vitro, depending upon the nature of the preparation and whether killing or inhibiting concentrations were sought. Generally such studies are complicated by the following technical difficulties: (a) inability to obtain bacteria-free cultures of trichomonads; (b) the limited solubility of some of the drugs tested; (c) osmotic pressure effects on trichomonads where high concentrations of salts were used; (d) the inhibiting effect of metabolic products of trichomonads and bacteria upon the organisms and the drug.

The present study of the chemotherapeutic efficacy of aldarsone, acetarsone, and carbarsone is based upon their relative inhibiting effects upon trichomonads in vitro and their relative toxicity. The inhibiting or trichomonadostatic values were determined by finding the lowest concentration of drug in culture media which prevented the growth of the flagellates. These included *Trichomonas hominis, T. vaginalis,* and *T. buccalis* from the bowel, vagina, and mouth of human beings,

*The writer is indebted to Dr. P. Brooke Bland and Dr. Norris W. Vaux for the facilities of their department and their constant interest during the course of this study.

respectively, and a cultivable trichomonad from the feces of a white rat, probably *T. parva.* The toxicity of the drugs was based on the maximum tolerated dose per kilogram when given to white rats per os.

TOXICITY STUDIES

Materials and Methods.—A comparative study was made of the toxicity of the three arsenicals. For purposes of this study the drugs were given per os since in the treatment of trichomonas infestations the drug is applied to mucous membrane surfaces such as the intestine or vagina.

A total of 87 healthy white rats were employed. The animals were under observation for a number of days before and at least twenty-one days after treatment. Each animal was weighed just prior to use and the dose was administered per kilogram of body weight. A solution of the drug to be tested was introduced into the stomach of the animal by means of a syringe and a piece of a fine ureteral catheter passed well into the esophagus of the rat.

TABLE I. TOXICITY OF ALDARSONE, ACETARSONE AND CARBARSONE PER OS IN RATS

DRUG	DOSE IN GRAMS PER KILOGRAM BODY WEIGHT	NUMBER OF ANIMALS	RESULTS	
			DIED*	SURVIVED**
Aldarsone (Aqueous solution)	1	1	0	1
	2	1	0	1
	3	1	0	1
	4	1	0	1
	5	1	0	1
	6	5	0	5
	8	6	1	5
	10	2	2†	0
	12	1	1	0
	15	1	1	0
Acetarsone (Acetarsone soluble—Abbott. Carbonated 0.7 gm. per gm. acetarsone)	2	1	0	1
	3	5	0	5
	4	5	3	2
	5	5	5	0
	6	2	2	0
	8	2	2	0
	10	1	1	0
Carbarsone (Carbonate 0.5 gm. per gm. of carbarsone)	3.0	2	0	2
	4.0	4	0	4
	5.0	5	1	4
	6.0	5	4‡	1
	6.5	5	4	1
	7.0	3	3	0
(Carbonate 1 gm. per gm. of carbarsone)	2	2	0	2
	3	2	0	2
	4	4	1	3
	5	3	3	0
	6	3	3	3
(Carbonate in excess)§	1	1	0	1
	2	1	0	1
	3	1	1	0
	4	1	1	0
	5	1	1	0

*Animals died within twenty-four hours unless otherwise indicated.

**Observed for at least twenty-one days.

†One died on second day.

‡One died on third day, another on fifth day.

§Exact amount not known but in excess of 1 gm. of carbonate per gm. of carbarsone.

To avoid the administration of large quantities the drugs were given in 10 to 20 per cent solution.

Aldarsone was used in aqueous solution since it is very soluble. Acetarsone was given in carbonated solution as acetarsone soluble* which contains 0.7 gm. of sodium carbonate per gram of acetarsone.

Carbarsone was used with several concentrations of sodium carbonate since early in the study it was observed that the proportion of carbonate materially influenced the toxicity of the preparation.

Results.—Table I shows that aldarsone was tolerated better than the other compounds. The maximum tolerated dose was in excess of 6 gm. per kilogram of body weight, and only 1 of 6 animals succumbed after receiving 8 gm. per kilogram.

The maximum tolerated dose of acetarsone soluble was less than 4 gm. per kilogram, since this amount was tolerated by only 2 of 5 rats; none of 5 rats succumbed after 3 gm. per kilogram.

Carbonated solutions of carbarsone did not yield entirely clear preparations, and for this reason various concentrations of sodium carbonate were tried. It was found, however, that the toxicity of the drug was increased by its addition. Thus with 0.5 gm. of carbonate per gram of carbarsone 4 of 5 rats tolerated 5 gm. per kilo and 1 of 5 rats tolerated 6 and 6.5 gm., respectively, while of 3 rats tested all succumbed to 7 gm. With equal parts of carbonate 5 gm. were not tolerated by any of 5 rats used, while 4 gm. were tolerated by 3 of 4 rats. When the carbonate was added in large excess only 2 gm. per kilogram were tolerated.

TRICHOMONADOSTATIC STUDIES

Materials and Methods.—The culture media employed routinely throughout the study consisted of Loeffler's dehydrated blood serum 0.4 per cent in a modified Ringer's solution (sodium chloride 6 gm., potassium chloride 0.1 gm., sodium bicarbonate 0.1 gm., calcium chloride 0.1 gm., distilled water 1,000 c.c.). The media were prepared fresh immediately before use. To quantities of culture media sufficient amounts of fresh stock solutions of the drugs were added to yield the desired concentration in the final mixture. The stock solutions of drugs were aldarsone 1 per cent in sterile distilled water, acetarsone 1 per cent in 1 per cent sodium bicarbonate solution, and carbarsone 1 per cent in 1 per cent sodium bicarbonate solution.

Ten cubic centimeters of the culture media-drug mixture were pipetted into culture tubes, which were then inoculated with 3 drops of active forty-eight-hour cultures of the flagellates. These were incubated at 37° C. and carefully examined for trichomonads at twenty-four-, forty-eight-, and seventy-two-hour periods.

The approximate concentration of each drug sufficient to prevent the growth of the flagellate tested was established after a number of trials, following which a series of ten concentrations closely graded on either side of the approximate value was prepared. These were similarly inoculated and examined. In this manner the concentrations of drug which just permitted and which just prevented growth were obtained. The latter was arbitrarily designated as the trichomonadostatic concentration, although the true value lies somewhere between the two.

Experiments were conducted on two strains of organisms for each of the four species of trichomonads studied; each experiment was performed three times.

Results.—In Table II are given the highest concentrations of drugs in which each strain of organisms tested survived, and the lowest concentration in which they were inhibited. It will be noted that in each experiment the required concentration of aldarsone was considerably lower than the respective figures for the other two drugs. The required concentrations of carbarsone were consistently slightly less than or equal to the acetarsone concentrations.

From the summarized results of Table III it will be seen that the average inhibiting or trichomonadostatic concentrations of aldarsone range from almost one-half to one-third that for acetarsone and carbarsone. Carbarsone in turn was slightly more effective than acetarsone.

*Acetarsone soluble is dispensed by the Dermatological Research Laboratories, Division of Abbott Laboratories, North Chicago, Ill.

Further examination of these tables indicates considerable variation in results not only among the trichomonads from the four different sources, but also among the two strains of each species studied; there was also moderate variation of the values for each experiment.

The lower values for *Trichomonas vaginalis* are in agreement with its general fragility in vitro; while the comparatively high figures for *Trichomonas parva* confirm our experience of the comparative resistance of this species to environmental factors, its easy cultivability and relative longevity in culture.

Those who have had experience in observing and cultivating trichomonads will not wonder at the variation in resistance of the two strains of each species tested. How much this is due to factors inherent in each strain of organism and how much to environmental factors, especially the accompanying bacteria, is difficult to estimate. The latter factor, however, is no doubt largely responsible for the variations in each set of readings for the same strain.

TABLE II. CONCENTRATIONS INHIBITING AND PERMITTING GROWTH

STRAIN	TESTS	ALDARSONE		ACETARSONE		CARBARSONE	
		ORGANISMS SURVIVED	ORGANISMS INHIBITED	ORGANISMS SURVIVED	ORGANISMS INHIBITED	ORGANISMS SURVIVED	ORGANISMS INHIBITED
		(CONCENTRATIONS IN MG. OF DRUG PER 100 C.C. CULTURE MEDIA)					
		Trichomonas vaginalis					
A	1	5.0	7.5	50	75	25	50
	2	5.0	7.5	50	75	25	50
	3	7.5	10.0	50	75	25	50
B	1	10	12.5	75	100	75	100
	2	25	50.0	100	125	75	100
	3	25	50.0	100	125	75	100
		Trichomonas hominis					
A	1	25	50	100	125	100	125
	2	25	50	150	175	150	175
	3	50	75	150	175	125	150
B	1	10	25	150	175	150	175
	2	25	50	75	100	75	100
	3	10	25	200	225	175	200
		Trichomonas buccalis					
A	1	25	50	75	100	50	75
	2	10	25	175	200	175	200
	3	50	75	150	175	100	125
B	1	50	75	175	200	75	100
	2	50	75	150	175	125	150
	3	75	100	200	225	150	175
		Trichomonas parva					
A	1	25	50	100	125	100	125
	2	50	75	150	175	125	150
	3	75	100	150	175	125	150
B	1	100	125	200	225	125	150
	2	75	100	225	250	200	225
	3	100	125	200	200	150	175

TABLE III. AVERAGE TRICHOMONADOSTATIC VALUES

	ALDARSONE (MG. PER CENT)	ACETARSONE (MG. PER CENT)	CARBARSONE (MG. PER CENT)
T. vaginalis	45	96	75
T. hominis	46	163	154
T. buccalis	67	179	133
T. parva	96	196	163

DISCUSSION

The pentavalent arsenicals, being less oxidizable than the trivalent series of products, and therefore more stable, are especially suitable for clinical use of surface infections and for oral administration.

In a personal communication, Raiziss[6] states that aldarsone (sodium-methylene-sulfonamino-hydroxy-phenyl-arsonate) and acetarsone (2-acetyl-amino-4-hydroxy-phenyl-arsonic acid) from their structural formulas are somewhat closer related to arsphenamine than carbarsone (p-carbamino-phenyl-arsonic acid). In addition to the arsonic acid group, carbarsone has a carboxylic acid group which is considered to be less therapeutic than the hydroxyl and amino groups which aldarsone and acetarsone have in common. In acetarsone the acetyl group is more firmly bound to the amino group than in the case of aldarsone in which the combination of the amino group with the methylene sulfonic acid group is firm.

Attempts to determine the direct killing power of the drugs for trichomonas by bringing relatively high concentrations of the drugs into contact with the organisms are not altogether satisfactory because of the insolubility of two of the preparations, acetarsone and carbarsone. Aldarsone, which is very soluble, was found by Bland and Rakoff[5] to destroy *Trichomonas vaginalis* in less than five minutes in a concentration of 1:30 and almost at once in a concentration of 1:10. Saturated solutions of a heavy suspension of acetarsone had little effect upon the organisms after a period of observation of one hour. Subsequent experiments have shown that suspensions of carbarsone also have little immediate effect upon the flagellates. Carbonated solutions of acetarsone 1:20 did not inactivate the organisms after one hour. More concentrated solutions of acetarsone and carbarsone require the addition of sodium carbonate in sufficient concentration to destroy the organisms by osmotic pressure effects alone.

Hegner and Eskridge[1] studied the effect of dilute carbonated solutions of carbarsone on cultures of *Trichomonas hominis*. They found that concentrations of 0.1 and 0.2 per cent killed the organisms within 4 days but not within two days, while concentrations of 0.3 and 0.5 per cent destroyed the organisms within two days. These results were confirmed by Gabaldon[2] who noted that carbarsone diluted in the culture fluid at a concentration of 0.3 per cent was lethal for *Trichomonas hominis* and a rat trichomonad, probably *T. para*, in less than seventy-two hours. In 0.05 per cent solutions death of all the organisms rarely occurred after an exposure of five days.

While studying the action of carbarsone on the cycle of development of *T. hominis* in culture, Gabaldon noted that in a concentration of 0.05 per cent an increase in the trichomonad population occurred in the first twenty-four hours, in 0.1 per cent solutions an increase rarely occurred, and in greater concentrations increases were never observed.

A comparison of these results with our observations confirms our belief that although the concentrations which we have designated as trichomonadostatic values are not sufficient to sterilize a healthy culture of the organisms in forty-eight or seventy-two hours, they will prevent the multiplication of the flagellates. The destruction of the organisms in the inoculum probably results from a number of factors in addition to the sub-lethal action of the drug, namely the inability of the organisms

to survive long without multiplication, their inability to produce resistant stages such as cysts, the action of bacteria upon the flagellates and the culture media.

The trichomonadostatic value has a definite practical significance in addition to affording an adequate means of comparison of the effect in vitro of the several drugs upon trichomonas. The most troublesome factor in attaining a permanent cure in the treatment of protozoan infestations is the prevention of recurrences after nearly all the organisms have been destroyed. In patients with trichomonas vaginitis, the eradication of all but a few of the organisms by mechanical means or by chemotherapy is easy of attainment; to destroy the few survivors which rapidly reinfest the vagina is frequently an annoying therapeutic problem. Indeed, the effectiveness of the dry form of treatment of trichomonas vaginitis with antiseptic powders is largely the result of the maintenance over a considerable period of time of a trichomonadostatic environment.

The comparative effective concentrations of the drugs with relation to their comparative toxicity merit consideration in view of the serious toxic effects which may result from absorption of large dosages. Although in the treatment of trichomonas vaginitis the pentavalent arsenicals are widely used by vaginal insufflation and in suppository form, more recently they also have been given by mouth. In the elimination of several intestinal protozoan infestations their administration per os is the rule.

Gabaldon[7] found that 150 mg. per kilogram of body weight was the minimal effective dose of carbarsone when given by mouth to infested rats each day for five consecutive days. It was found that this yielded a percentage concentration of carbarsone in the large intestines estimated to be 0.47. A carbarsone concentration of 0.3 per cent killed rat trichomonads within twenty-four to forty-eight hours in vitro, supporting the belief that, in rats, carbarsone acts upon trichomonads directly, as it appears to do in cultures.

It is questionable whether a concentration of 0.3 per cent carbarsone can be reached in the intestine of human beings with the dosages recommended for oral use even when used over a prolonged period of time.

The marked increase in the toxicity of carbarsone following the addition of sodium carbonate to increase its solubility, as found during the course of this study, is noteworthy. The increase in toxicity is apparently proportionate to the concentration of carbonate. The clinical importance of this observation, especially when the drug is taken internally is apparent. The effect of sodium carbonate upon the pentavalent arsenicals, especially the insoluble members, acetarsone and carbarsone, requires further investigation.

In a recent study Armaghan[8] has shown that in rats infected with Giardia a dose of 0.75 gm. of aldarsone per kg. of body weight, which is less than one-tenth the maximum tolerated dose, seemed adequate to effect a cure in most animals.

NOTE: Chemotherapeutic data including the toxicity of a number of pentavalent arsenicals and their effect upon trichomonads in vitro and in vivo have appeared in a study by Nelson and Tatum (J. Pharmacol. & Exper. Therap. 63: 122, 1938). Among 10 pentavalent arsenicals tested were acetarsone, carbarsone, tryparsamide

and mapharsen. These workers also noted a higher therapeutic index for carbarsone than for acetarsone, while tryparsamide was apparently the most effective. So far as we know, aldarsone was not included in their study.

Armaghan and Mediary (Am. J. Hyg. 27: 250, 1938) have recently published data indicating that aldarsone is of value in the treatment of infestations with a number of intestinal protozoa in man, including *T. hominis*.

The pentavalent arsenicals when administered per os to white rats are not highly toxic, being tolerated in doses of 2 gm. per kilo or more. In other laboratory animals, however, these drugs are not tolerated nearly so well.

In view of these findings the considerably lower toxicity of aldarsone, when tested on white rats, indicates that it is to be preferred to acetarsone or carbarsone for the treatment of protozoan infestations. In the treatment of trichomoniasis it has the further advantage of a higher trichomonadicidal value when tested in vitro.

It may be concluded that the chemotherapeutic index of aldarsone in the treatment of trichomonas infestations is several times greater than that of acetarsone or carbarsone by virtue of its more effective action against the parasite and its lower toxicity for the host.

SUMMARY

1. A comparison of the chemotherapeutic efficacy of aldarsone, acetarsone, and carbarsone in the treatment of trichomonas infestations was made, based upon their relative inhibiting effects upon trichomonads in vitro and their relative toxicity for rats.

2. The toxicity of the drugs was based on the maximum tolerated dose per kilogram when given to rats per os.

Aldarsone was tolerated better than the other compounds, the maximum tolerated dose being in excess of 6 gm. per kilogram of body weight, while only one of six animals succumbed to 8 gm. per kilogram.

3. The maximum tolerated dose of acetarsone soluble was more than 3 but less than 4 gm. per kilogram of body weight.

4. The toxicity of carbarsone varied with the amount of carbonate used in preparing the solution. Thus with 0.5 gm. of carbonate per gram of carbarsone 4 of 5 rats tolerated 5 gm. per kilogram of body weight; with equal parts of each 5 gm. were not tolerated by any of 5 rats, while 4 gm. were tolerated by 3 of 4 rats; when the carbonate was added in excess only 2 gm. per kilogram were tolerated.

5. The inhibiting or trichomonadostatic values were determined by finding the lowest concentration of drug in culture media which prevented the growth of the flagellates; these included *Trichomonas vaginalis, T. hominis,* and *T. buccalis* from the vagina, bowel, and mouth of human beings, respectively, and a cultivable trichomonad from the feces of a white rat, *T. parva.*

6. The average trichomonadostatic concentrations of aldarsone ranged from about one-third to one-half that for acetarsone and carbarsone. Carbarsone was slightly more effective than acetarsone.

7. *Trichomonas vaginalis* was considerably more susceptible to the pentavalent arsenicals than were the other species; the inhibiting con-

centration of aldarsone was 45 mg. per cent (1:2220), of acetarsone 96 mg. per cent (1:1040), of carbarsone 75 mg. per cent (1:1330).

Trichomonas hominis, T. buccalis, and *T. parva* showed greater resistance to the arsenicals in the order named.

8. It is concluded that of the three pentavalent arsenicals, aldarsone has by far the highest chemotherapeutic index in the treatment of trichomonas infestations, while carbarsone is somewhat more effective than acetarsone.

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TREATMENT OF PELVIC INFLAMMATION BY THE IONTOPHORESIS OF A CHOLINE COMPOUND*

Adolph Jacoby, M.D., F.A.C.S., New York, N. Y.

(From the Department of Gynecology, New York Post-Graduate Medical School and Hospital, Columbia University)

IN A previous communication, the underlying principles upon which the treatment of pelvic inflammatory conditions by iontophoresis is based, together with the technique and the results obtained in 10 patients, were described.[1]

This report reviews the treatment of 50 patients by the same method.

The original technique has been changed so that at the present time 20 c.c. of a 0.5 per cent solution of acetyl-beta-methycholine-chloride† is used instead of a 1 per cent solution. The vaginal electrode has also been modified, so that it now consists of a thin cylindrical shaft, 3/8 of an inch in diameter and 8 inches long, to one end of which is attached by a central pivot a thin bar 2 inches long and 3/8 of an inch wide. The proximal end of the shaft has a terminal for the attachment of the conducting cord.

Gauze, saturated with a 0.5 per cent solution of acetyl-beta-methylcholine-chloride, is placed over the bar on the distal end of the electrode and then introduced into one side of the posterior vaginal fornix. Pressure on the other end of the electrode swings the bar across the vaginal fornix. The ends of the gauze are then firmly tucked into the vaginal fornices around the bar of the electrode. The speculum is withdrawn and the positive pole of the galvanic current attached to the vaginal electrode. The negative pole is attached to a well-moistened felt pad, 6 inches square, which is placed on the lower abdomen. Fifteen milliamperes of current are applied for twenty minutes.

Of the 50 patients treated, 11 were operated upon after treatment, 4 were treated after a preceding operation for other conditions, and the remaining 35 received treatment only and were at no time subjected to any operative procedure.

The average age of these patients was 29 years, the youngest being 19 years old and the oldest 46. Forty-five women were married and five were single. The

*Read at the Academy of Medicine, Section of Obstetrics and Gynecology, January 25, 1938.

†The acetyl-beta-methylcholine-chloride (mecholyl) was supplied by Merck & Co., Inc.

chief symptoms presented by this group of patients were pain in the lower abdomen, in one or the other quadrants, and back. Thirty-three had urinary frequency, 36 cervical discharge, and 9 dysmenorrhea and some menstrual irregularity. Seven had fever of 101° F. or over, prior to the institution of treatment.

In this series of patients, those having any pelvic mass or thickening, whether due to inflammation with or without additional pathology, or whether noninflammatory, were treated, in an attempt to determine the limitations of the modality. The diagnoses, the number of treatments given, the time of treatment, and the results obtained are shown in Table I.

Fig. 1.—Position of movable bar for introduction into the vaginal fornix.

Fig. 2.—Position of movable bar after introduction.

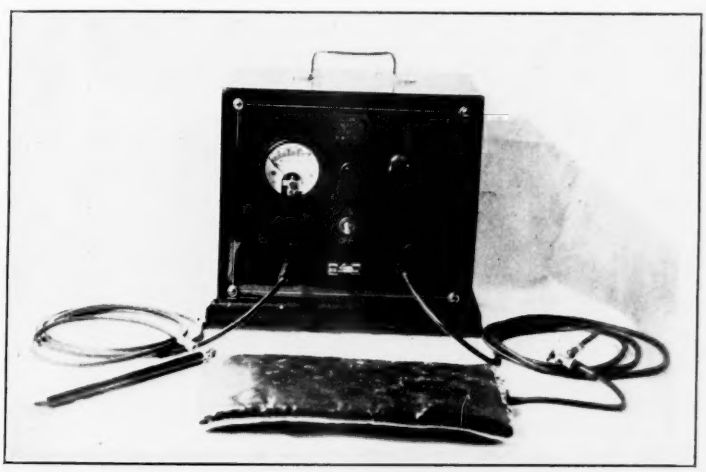

Fig. 3.—Outfit required for iontophoresis.

In 11 patients who were subjected to operation after treatment with iontophoresis, eight had an association of salpingo-oophoritis with other pathological conditions. At operation it was found that the inflammatory exudate had subsided, but that the additional pathology, as shown in Table II, remained unaltered and appropriate operative treatment was therefore instituted. In three other patients, iontophoresis was given for variable lengths of time to determine the nature of the existing masses. No beneficial results were obtained by the treatment, and at operation the pathologic conditions indicated in Table II were found.

TABLE I. NONOPERATED

	NO. OF CASES	NO. OF TREATMENTS			TIME (IN DAYS)			RESULT				REMARKS
		LEAST	MOST	AVERAGE	EARLIEST	LATEST	AVERAGE	CURED	RELIEF	NO CHANGE	RECURRENCE	
Pelvic Inflammation												
Salpingo-oophoritis	20	3	19	7	5	32	20	17	1	2	3	Exudate completely disappeared in cases cured
Salpingo-oophoritis, ovarian cyst	3	4	20	10	30	65	48	--	3	--	--	Exudate disappeared; cyst, no effect
Salpingo-oophoritis, retroversion, Nabothian cyst	4	1	12	7	2	60	43	--	4	--	--	Exudate disappeared; Nabothian cyst and retroversion, no effect
Salpingo-oophoritis, cervicitis, Nabothian cyst	3	7	9	8	16	39	26	--	3	--	--	Exudate disappeared; Nabothian cyst, no effect
Salpingo-oophoritis, Nabothian cyst, Bartholin abscess	1	6	--	6	22	--	22	--	1	--	--	Exudate disappeared; abscess opened
Salpingo-oophoritis, Nabothian cyst, gonorrhea, ovarian cyst	1	9	--	9	18	--	18	--	1	--	--	Exudate disappeared; ovarian cyst, no effect
No Pelvic Inflammation												
Fibroid, cervicitis, Nabothian cyst	1	7	--	7	31	--	31	--	--	1	--	Mass and cysts unchanged
Pregnancy, gonorrhea	1	14	--	14	46	--	46	--	--	1	--	No effect on gonorrhea or pregnancy
Retroversion, prolapsed ovary	1	27	--	27	120	--	120	--	--	1	--	No effect
Pelvic hematoma, following preceding operation	4	12	28	19	40	240	122	--	--	4	--	Slight diminution in size only

TABLE II. OPERATED

	NO. OF CASES	NO. OF TREATMENTS			TIME (IN DAYS)			RESULT				REMARKS
		LEAST	MOST	AVERAGE	EARLIEST	LATEST	AVERAGE	CURED	RELIEF	NO CHANGE	RECURRENCE	
Pelvic Inflammation												
Salpingo-oophoritis, plus other pathology associated with: Ovarian cysts 3, Fibroid 1, Retroversion 1, Abscess 1, Prolapsed ovary 1, Hydrosalpinx 1	8	2	20	9	4	98	42	--	8	--	--	Exudate gone; coexisting pathology, unchanged
No Pelvic Inflammation												
Carcinoma of ovary and sigmoid	1	8	--	8	19	--	19	--	--	1	--	Differential diagnosis
Fibroid, ovarian cyst	1	4	--	4	9	--	9	--	--	1	--	Differential diagnosis
Ovarian cyst	1	12	--	12	150	--	150	--	--	1	--	Differential diagnosis

TABLE III

	NO. OF CASES	NO. OF TREATMENTS			TIME (IN DAYS)			RESULT			
		LEAST	MOST	AVERAGE	EARLIEST	LATEST	AVERAGE	CURED	RELIEF	NO CHANGE	RECURRENCE
Pelvic Inflammation											
Nonoperated	32	1	20	7.4	2	65	26.1	17	13	2	3
Operated	8	2	20	9.0	4	98	42.0	--	8	--	--
No Pelvic Inflammation											
Nonoperated	7	7	28	17.7	31	240	97.8	--	--	7	--
Operated	3	4	--	8.0	9	--	59.3	--	--	3	--

DISCUSSION AND SUMMARY

It has been repeatedly demonstrated that hyperemia is an important factor in the treatment and elimination of inflammation. In the pelvis, hyperemia may be induced by various measures, such as douches, the vaginal hot water bag (Elliott), external heat, diathermy and short wave currents. It has been demonstrated that acetyl-beta-methylcholine-chloride introduced by iontophoresis initiates a hyperemia of from four to eight hours' duration, and this action was relied upon to effect a definite result in cases of pelvic inflammation. My experience with this therapeutic method has verified the correctness of these premises (Table III).

Of the 50 patients treated, 40 had varying degrees of inflammation of one or both adnexa, with or without additional pathology. Twenty of these 40 cases had adnexal inflammation only. In 17 of these 20, complete remission of the inflammation occurred with a disappearance of symptoms and an apparent restitution of the structures to normal. In the other 20, in every instance the inflammatory exudate disappeared, but the associated pathologic conditions remained unaffected. In 8 of the group with associated pathology, we were able to demonstrate at a subsequent operation the existence of the residual pathology. In the group of 10 cases in which there was no satisfactory result after adequate periods of treatment, 3 patients were operated upon, and in these the masses were found to be noninflammatory. The diagnosis in the 7 not operated upon, is shown in Table I.

CONCLUSION

From the foregoing, it is evident that whenever the pelvic pathology consists of an exudative inflammatory process, a prompt recession and restoration to normal occurs following treatment by iontophoresis of acetyl-beta-methylcholine-chloride. On the other hand, if the pathology includes organized inflammatory products or definite pathologic tissue alteration, such as cysts, or tumors, no change is produced.

It is reasonable, therefore, to conclude that in the method of treatment by iontophoresis of acetyl-beta-methylcholine-chloride, we have a therapeutic means of differential diagnosis of pelvic masses, as well as an efficient modality for the rapid cure of pelvic exudative inflammation in any stage.

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151 West Seventy-Seventh Street

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Hammar found reports of 18 theca cell tumors in the literature and adds a case of his own. His patient was 20 years old and in her the tumor produced an amenorrhea.

J. P. Greenhill.

A COMPARATIVE STUDY OF THE EFFECTIVENESS OF TWO ANTISEPTICS IN PREVENTING INFECTION FOLLOWING DELIVERY

With a Report on 1,000 Cases

John E. Tritsch, M.D., F.A.C.S., New York, N. Y.

(From the Department of Obstetrics and Gynecology of the Metropolitan Hospital)

THIS report is contributed in the interest of aiding in the evaluation of a new antiseptic by comparing it with one which is accepted for obstetric use. The new antiseptic, a soluble concentrate of synthetic alkyl and halogen phenol derivatives* was compared with mercurochrome (dibromo-oxymercuri-fluorescein-sodium).

Some information as to the antiseptic and germicidal potency of the new product may be gained from Table I of minimum germicidal concentrations destructive for a number of common pathogenic microorganisms according to experiments conducted in the manufacturers' laboratories.

Table I

MICROORGANISM	TEMPERATURE	MINIMUM GERMICIDAL CONCENTRATIONS IN 10 MIN.
Staph. aureus	20° C.	1:300
Staph. aureus	37° C.	1:700
Strept. (Hemolytic)	37° C.	1:750
Strept. viridans	37° C.	1:1400
B. coli	20° C.	1:900
B. typhosus	20° C.	1:1000
B. pyocyaneous	37° C.	1:350

Among other things, this table indicates the antiseptic effect of "amphyl" upon pyogenic cocci, which play a role in both ante- and post-partum complications, and shows that these microorganisms are killed by comparatively low concentrations.

A total of 1,000 cases were studied; in 500 cases mercurochrome was utilized, and in the other 500 cases amphyl was used. Mercurochrome was used according to the technique suggested by Mayes, and amphyl was used as a 5 per cent tinted aqueous solution for external painting, and as a 2 per cent aqueous solution for vaginal instillation.

The technique was as follows:

1. The external genitals were shaved and scrubbed with tincture of green soap.

2. The external genitals and adjacent area of the thighs and abdomen were painted or sprayed with a De Vilbis atomizer, using a tinted solution of 5 per cent amphyl in the one group and an aqueous-alcohol-acetone solution of mercurochrome in the other.

3. Utilizing the syringe suggested by Mayes, 3 drams of the aqueous 2 per cent solution of amphyl in the one group, and of a 4 per cent mercurochrome solution in

*Amphyl furnished through the courtesy of the Lehn & Fink Products Corporation.

the other, were injected into the vagina. The injection was made at a depth of from 4 to 5 inches; the point of the syringe was kept close to the vaginal floor and the barrel close to the pubis. The labia were held firmly together around the syringe while the contents were being injected, in order to distend the vagina with the solution and to prevent loss of the solution, as much as possible.

The routine up to this point was followed in each case upon admission.

4. The instillation of mercurochrome and amphyl and external painting were repeated every twelve hours during labor, and prior to all vaginal examinations done during labor.

5. Before draping in the delivery room, the parts were cleansed and then sprayed or painted with the aqueous-alcohol-acetone solution of mercurochrome or with the tinted 5 per cent solution of amphyl. The perineum was then depressed and 2 drams of the solution were put into the vagina.

6. At the conclusion of the delivery, a solution of 2 per cent amphyl or a 4 per cent solution of mercurochrome, in water was instilled into the vagina.

7. These solutions were also instilled into lacerations and episiotomy wounds before repair.

The standard of morbidity utilized in this discussion is identical with that used by Mayes, viz., "a rise in temperature to 100.4° F. on two consecutive days, not including the first twenty-four hours, and occurring on or before the tenth day." These temperatures are taken by mouth every four hours.

The distribution of cases in each group was as follows:

Amphyl group of primiparas	173 cases
Amphyl group of multiparas	327 cases
Mercurochrome group of primiparas	183 cases
Mercurochrome group of multiparas	317 cases

The average age of the patients in both series showed very little variation. Amphyl group of primiparas average 22.03 years and mercurochrome group of primiparas 22.11 years. Amphyl group of multiparas averaged 23.8 years and mercurochrome group of multiparas, 22.72 years.

The number of internal examinations done, also ran rather closely parallel. In rectal examinations there were 3.34 per patient in amphyl group of primiparas, and 3.33 in mercurochrome group of primiparas. There were 3.24 per patient in amphyl group of multiparas and 2.45 in mercurochrome group of multiparas.

In vaginal examinations, there were 0.092 per patient in amphyl group of primiparas, and 0.18 in mercurochrome group of primiparas; 0.079 in amphyl group of multiparas and 0.07 in mercurochrome group of multiparas.

Table II indicates the average time elapsing between the rupture of membranes to the delivery, the average length of time from the last instillation of antiseptic solution to delivery, the average duration of labor, and the average number of instillations.

These figures do not show any striking differences and are little more than of academic interest.

Table III is a tabulation of the spontaneous and operative incidence in the deliveries.

TABLE II

	AMPHYL		MERCUROCHROME	
	PRIM.	MULT.	PRIM.	MULT.
Time from rupture of membranes to delivery	4.46 hr.	3.04 hr.	5.61 hr.	4.32 hr.
Time from last instillation to delivery	7.51 hr.	6.59 hr.	8.43 hr.	5.77 hr.
Duration of labor	14.85 hr.	10.14 hr.	15.98 hr.	11.33 hr.
Number of instillations per patient	1.20	1.09	1.28	1.10

TABLE III

TYPE OF DELIVERY	AMPHYL		MERCUROCHROME	
	PRIM.	MULT.	PRIM.	MULT.
Spontaneous	149 (86.2%)	305 (93.3%)	134 (73.4%)	301 (95.0%)
Low forceps	18 (10.3%)	5 (1.5%)	27 (14.7%)	2 (0.6%)
Midforceps	1 (0.6%)	2 (0.6%)	6 (3.3%)	2 (0.6%)
High forceps	0	1 (0.3%)	0	0
Breech extraction	3 (1.7%)	10 (3.1%)	11 (5.9%)	8 (2.5%)
Cesarean section	1 (0.6%)	3 (0.9%)	5 (2.7%)	1 (0.3%)
Vaginal cesarean section	0	0	0	1 (0.3%)
Version	1 (0.6%)	1 (0.3%)	0	2 (0.6%)

From Table III it appears that there was slightly more operative procedure in the mercurochrome group than in the amphyl group.

Table IV shows incidence of perineal injury.

TABLE IV

	AMPHYL		MERCUROCHROME	
	PRIM.	MULT.	PRIM.	MULT.
Episiotomy	52 (29.9%)	2 (0.6%)	78 (40.8%)	2 (0.6%)
1° Laceration	28 (16.1%)	52 (15.8%)	42 (22.8%)	52 (16.3%)
2° Laceration	17 (9.8%)	20 (6.1%)	13 (7.1%)	16 (5.0%)
3° Laceration	0	0	0	1 (0.3%)

The gross and net morbidity are indicated in Table V.

It is evident from Table V that the difference between the groups is practically negligible. In the amphyl group of 500 cases there were 31 morbid cases of presumably birth canal origin or an incidence of 6.2 per cent, while in the mercurochrome group, there were 32 morbid cases, an incidence of 6.4 per cent. Also it is shown here that the infection incidence in primiparas is 9.2 per cent and in multiparas 4.6 per cent.

TABLE V

	AMPHYL		MERCUROCHROME	
	PRIM.	MULT.	PRIM.	MULT.
Gross	20 cases	22 cases	20 cases	20 cases
Eliminated (not birth canal injections)	4 cases	7 cases	3 cases	5 cases
Net	16 cases (9.25%)	15 cases (4.5%)	17 cases (9.29%)	15 cases (4.7%)

The cases eliminated from the gross morbidity were only those in which an extra birth canal origin could definitely be ascertained, and below are indicated the numbers of cases and causes of morbidity in the exempted cases.

AMPHYL

Primiparas (4 cases):

1. Influenzal pneumonia (present on admission)
2. Osteoperiostitis, internal tuberosity right knee (present on admission)
3. Upper respiratory infection (present on admission)
4. Temperature before delivery, unknown origin, profound secondary anemia

Multiparas (7 cases):

1. Abscess of face (secondary to tooth infection)
2. Acute mastitis
3. Cellulitis of the thigh
4. Pyelitis
5. Pericarditis with effusion
6. Upper respiratory infection with bronchitis
7. Acute enteritis

MERCUROCHROME

Primiparas (3 cases):

1, 2, 3. Acute mastitis

Multiparas (5 cases):

1. Pyelitis
2. Acute pulmonary tuberculosis
3. Dental abscess
4, 5. Acute mastitis

The duration of morbidity in each group is designated in Table VI.

TABLE VI

DAYS	AMPHYL		MERCUROCHROME	
	PRIM.	MULT.	PRIM.	MULT.
2	1	2	1	6
3	6	8	2	5
4	3	1	3	2
5	2	0	4	1
6	3	0	1	0
7	0	0	2	1
8	0	1	1	0
9	0	1	0	0
10	0	1	0	0
11	1 (died)	0	1	0
12	0	0	0	0
13	0	0	0	0
14	0	0	1	
15	0	0	0	
16		1	1	
Totals	16	15	17	15

The average length of morbidity in each series was as follows: Amphyl group of primiparas 3.85 days, multiparas 4.93 days. Mercurochrome group of primiparas 6.66 days, and multiparas 3.12 days.

The morbidity in amphyl group of primiparas includes the death which occurred on the eleventh day and has been included as an eleven day morbidity.

In the entire series of 1,000 cases, the number of spontaneous and operative deliveries are shown in Table VII, also the incidence of infection in each.

TABLE VII

TYPE OF DELIVERY	CASES	INFECTION	PERCENTAGE	
Spontaneous	889	48	5.4%	
Low forceps	52	6	11.5%	7.4%
Midforceps	11	1	9.0%	
High forceps	1	0	0	
Breech extraction	32	1	3.1%	
Abdominal cesarean section	10	7	70.0%	
Vaginal cesarean section	1	0	0	
Version (podalic)	4	0	0	
Totals	1000	63	6.3%	

CONCLUSIONS

1. It is evident from the preceding that the amphyl and mercurochrome techniques are about of equal efficiency in the prevention of puerperal infection.

2. The incidence of infection was definitely less in spontaneous deliveries (5.4 per cent) than operative deliveries (7.4 per cent), and twice as great in primiparas as in multiparas and at least part of this is undoubtedly due to the greater incidence of operative deliveries in primiparas (9.2 per cent), than in multiparas (4.6 per cent).

3. Under conditions where economy is important, amphyl, being less expensive, might be preferable.

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1000 PARK AVENUE

Foederl, Viktor: Pathology and Clinical Course of Disgerminoma Ovarii, Arch. f. Gynäk. **165:** 392, 1938.

From a study of 13 cases of disgerminoma ovarii in the Vienna Frauenklinik, the author concluded that the malignant character of this tumor cannot be questioned. These newgrowths are malignant microscopically, have marked powers of invasion and produce metastases into other pelvic structures and through the lymphatics into the retroperitoneal spaces, early and rapidly. Careful microscopic studies showed downgrowth through the basal membrane in almost every instance. In addition, tumor cells could be found in the lymphatics and the blood vessels of the hilus. The tumor capsules also showed perforation by the tumor cells. Foederl believes that both granulosa cell tumors and disgerminoma arise from indifferent mesenchymal cells.

RALPH A. REIS.

THE USE OF BLOOD TRANSFUSIONS IN THE TREATMENT OF PYELITIS COMPLICATING PREGNANCY

LOUIS H. DOUGLASS, M.D., F.A.C.S., AND KENNETH LAUGHLIN, A.B., M.D.,
BALTIMORE, MD.

(From the Department of Obstetrics of the University of Maryland, School of Medicine and the Obstetrical Division of the Baltimore City Hospitals)

THE frequency of pyelitis complicating pregnancy is usually greatly underestimated, there being several reasons for this. Many of the attacks are mild and have a tendency to subside spontaneously, so that they are either not reported or are undiagnosed. Only the individuals with more severe cases are admitted to the hospitals and even in reports from these institutions are found discrepancies.

For example, Traut said that pyelitis occurred twice in each 100 pregnant women at the New York Hospital and the expectancy for obtaining a nonviable infant from women suffering from this condition is 3 times as great as in normal pregnancy, while abortions, premature labors and full-term stillbirths are common. Their fetal mortality was 10 per cent, as compared to their clinic fetal mortality of 3.3 per cent. Mussey found evidence of some degree of pyelitis in 20 per cent of all pregnant women. DeLee says that two-thirds of all women dying during pregnancy have had pyelitis at some time, while Baird found signs of infection in 42.5 per cent in 1,000 cases studied and Emge reported an incidence of 7 per cent.

The treatment of a condition occurring with such frequency and followed by the well-known and serious sequelae should command attention. The fact that many are concerned with this problem is well illustrated by the voluminous literature which has collected in recent years, and the several new methods of treatment which have been advocated. It is the purpose of this short paper to call attention to what must be a well-known but hitherto unmentioned adjunct in treatment; i.e., blood transfusions.

It has been our experience at the Baltimore City Hospitals and the University Hospital, Baltimore, that the patient who has a resistant form of pyelitis almost always has a very definite anemia, this anemia becoming more severe as the condition advances. It is our opinion that the disease is either an etiologic or a decidedly aggravating factor in this anemia and that the anemia itself so lessens the resistance of the patient to infection that little improvement from the pyelitis can be expected until it is overcome. Therefore, in addition to the recognized and accepted forms of treatment, we have added in recent years the practice of carefully watching for anemia, and, when found, of giving blood transfusions. The amount of blood at any one transfusion is usually small, 150 c.c. to 250 c.c., but they are repeated at intervals of a few days until the patient shows definite evidence of improvement.

Should it be decided to treat the patient with sulfanilamide, transfusions become even more necessary, and it should be the rule that the treatment should not be begun until the patient's red blood count and

hemoglobin have been brought to a safe level. Also as the treatment continues there should be daily determinations and an available donor should always be held in readiness.

With this addition to our therapy, we have found (1) a 30 per cent reduction in hospitalization, (2) a much lessened instance of ureteral catheterization and drainage, and (3) an entire absence of the necessity for therapeutic abortion.

The following are a few case histories which illustrate the beneficial effects of even one or two small blood transfusions:

CASE 1.—M. T., a 22-year-old primigravida, was admitted to the University Hospital Aug. 26, 1937. Her past and family histories were noncontributory, and her prenatal course was apparently normal until August 20, one week before admission, when she noticed some frequency of urination with burning, pain in the right kidney region and fever and chills. On August 23 her temperature reached 104° F. and the urine contained numerous pus cells. She was treated at home with forced fluids, alkalinization of the urine, postural drainage, and bed rest. Patient improved slightly under this, but her tenderness, fever, and pyuria persisted, and she was hospitalized. On admission her temperature was 100.6° F. and her urine contained a few white blood cells with clumping. The blood chemistry was normal and the blood culture negative. The urine culture was positive for colon bacillus. The blood count on admission revealed a moderate secondary anemia with a red blood count of 3,890,000 and a hemoglobin of 74 per cent. Alkalinization and postural drainage were continued and the patient was given a blood transfusion of 300 c.c. of citrated blood. On the day of admission her temperature reached a maximum of 102° F., following which it subsided to normal on the third day and remained normal thereafter. Subsequent urinalyses revealed many clumped white blood cells, and the patient lost all of her subjective symptoms. She was discharged in good condition, the urine at this time showing no pus cells and the urine culture being negative.

In this case it would appear that the course of the disease was decidedly shortened and that treatment was held to a minimum of simple, safe procedures.

CASE 2.—E. H. This patient, a 16-year-old secundigravida, was admitted to the University Hospital Apr. 12, 1937, from the Out-Patient Department in the thirtieth week of her pregnancy because of pyelitis and anemia. Her past and family histories were noncontributory and her previous pregnancy and labor had been normal and uneventful. She was first seen in the prenatal clinic July 14, at which time she seemed normal and remained so until August 1, when she developed pain in the left lumbar region. This pain was accentuated on urination, and at the same time she noticed that her urine had become very cloudy. When the urine was examined many pus cells were found. Therefore she was treated on the Outside Service with alkaline therapy and forced fluids. Under this regime she became comfortable but the urine continued to contain many pus cells in clumps and the blood count showed only 2,620,000 red blood cells and a hemoglobin of 48 per cent. Because of these findings she was admitted to the hospital for further treatment of the pyelitis as well as treatment of the anemia. At the time of admission her urine contained many pus cells. Urine culture was positive for *B. coli*, and the blood culture was negative. She was placed on the regime of forced fluids, urine alkalinization, and antianemia diet. After several days she showed no improvement and was given two transfusions on alternate days consisting of 400 c.c. of whole citrated blood each time. On August 28 her red blood count had increased to 3,480,000 with a hemoglobin of 78 per cent; urine contained no pus cells and temperature was normal. At the time of discharge on August 30, she was in good condition. The urine culture taken on that day showed no growth after five days. The patient went through the remainder of her pregnancy without any further attacks and six months later was clinically well.

In this case the subsidence of the subjective symptoms was not accompanied by clinical evidences of improvement, and it was only after blood transfusions that the urine became negative. It may be assumed that in this case the patient was saved a latent or chronic type of infection. The case was unusual also in that the symptoms were referable first and last to the left urinary tract alone.

CASE 3.—M. M. This patient, a 22-year-old primigravida, was admitted to the hospital May 10, 1937. This was her second admission, the first having been just a few days before and for the same reason, that is, pyelitis complicating a pregnancy of twenty-five weeks' duration. The patient was quite uncomfortable when she entered the hospital, her temperature was fluctuating between 103° F. and subnormal, and the urine contained a fair number of pus cells with clumping. On admission the blood chemistry was normal, blood culture negative, but the urine culture positive for *B. coli*. She was placed on routine treatment but showed little or no improvement, and on May 27 she was given 300 c.c. of whole citrated blood. This was followed on June 1 by a second transfusion of 350 c.c. after which her condition immediately improved, and on June 4 she was allowed out of bed and on June 6 she was discharged. At full term she was readmitted to the hospital and delivered of a normal living child. At this time there were no signs or symptoms of pyelitis present.

SUMMARY AND CONCLUSIONS

1. Pyelitis is a very frequent complication of pregnancy, probably occurring in varying degrees of severity in about 25 per cent of all pregnant women.

2. The condition frequently is quite resistant to the ordinary methods of treatment.

3. In many cases if the blood is examined, there is found a definite, and at times severe anemia associated with the pyelitis. The anemia in turn lessens the patient's resistance, and a vicious cycle is thus established, which, unless broken, renders her recovery difficult.

4. A rational and rather safe answer to the problem is found in blood transfusions of fairly small amounts and repeated at intervals until improvement of both the anemia and pyelitis occurs.

5. Transfusions should prove to be especially valuable in those patients treated with sulfanilamide.

6. Three illustrative cases are presented.

Picinelli, G.: On the Therapeutic Value and the Conservability of Placental Blood, Arch. di ostet. e ginec. 2: 83, 1938.

The author points out that the introduction of small transfusions and the increasing variety of their use stimulate new sources of blood. Mentions the use of cadavers' blood as proposed by Judine. The idea which simultaneously developed in Italy and other foreign countries of the utilization of umbilical cord blood for transfusion is practical.

He demonstrates and emphasizes the higher erythropoietic value of placental blood when contrasted to that obtained from the pregnant woman or normal man. He describes the technic of obtaining blood from the umbilical cord and for its preservation, and finds that it may be kept from six to eight days.

A. A. MARCHETTI

BLOOD SUGAR CHANGES IN LABOR AND AFTER DELIVERY

ALLEN LEDYARD DECAMP, B.S., M.D., FAYETTEVILLE, N. C.
(From Kensington Hospital for Women, Philadelphia, Pa.)

IT IS a well-known fact that hyperglycemia is common after exercise associated with emotional stress.[1] Rowe and McManus[2] report that low blood sugar levels persist "actually during labor and to within a few minutes of delivery. There is a marked rise in blood sugar on emptying the uterus." Our results do not agree, particularly with respect to labor levels.

The original impetus for this work came from our harrowing experiences with two cases of an atypical form of shock. Shock occurred in each case about an hour after delivery, manifested by a weak and often imperceptible pulse; a blood pressure that dropped to 30 and 40 mm. systolic; cold moist extremities; but a fully conscious, comparatively comfortable patient, without air-hunger or any other complaint. In both cases hemorrhage was ruled out and supportive measures in the form of intravenous glucose in normal saline, and massive doses of suprarenin (in the second case 30 c.c. were used over a period of six hours) were resorted to with the result that both patients snapped out of their "shock" and eventually recovered.

In attempting to find an explanation for their behavior the question of hyperinsulinism came up. Though this could be ruled out on the basis of the lack of response to large quantities of glucose administered intravenously, we found that the literature is notably barren on the subject of blood sugar during pregnancy, labor, and immediately after delivery, and we decided to investigate.

After starting this work a paper by Adair and others[3] entitled "Vascular Collapse in Toxemia of Pregnancy" completely explained one of our cases of "shock," but left us as much in the dark as ever about the other.

Our subjects were selected at random from two of our A. M. prenatal clinics. Blood specimens were taken at each clinic visit, at the same hour, approximately four hours after their respective breakfasts. The average of these figures was taken as each patient's normal. General average proved to be 87 mg. per 100 c.c.

METHOD

After admission to the hospital in labor, a specimen of blood was taken approximately fifteen to thirty minutes before delivery, and another thirty to sixty minutes after the termination of the third stage. For a time fasting sugars were taken on the morning of discharge, but these proved to be so near the predetermined average, that this determination was dispensed with.

From 50 patients originally selected only 25 studies are complete enough to be considered in this report.

There were 6 primiparas and 19 multiparas. Twenty women delivered spontaneously and outlet forceps operations were done on 5. Twelve patients received

only nembutal gr. ivss-vi; 6 had morphine-scopolamine narcosis and an inhalation anesthetic. Seven women required neither analgesia nor anesthesia.

Of the 6 primiparas, all had morphine-scopolamine narcosis; 4 had open-drop ether at the end of the second stage, one gas-oxygen-ether, and the last gas-oxygen. Five of the 6 were delivered with outlet forceps. Their average time in labor was eighteen and one-half hours. The normal blood sugar average in this group was 87.5 mg. The average during labor was 111 mg., a rise of 26.8 per cent. The average in the postdelivery determinations was 115 mg., or a 31.4 per cent rise above average normal.

The 19 multiparas had no inhalation anesthetics; their average duration of labor was eight and one-half hours. Normal average of blood sugar levels was 85.6 mg.; average during labor 107 mg., a 25 per cent rise. Postdelivery average was 119.5 mg., or a 39.8 per cent rise above average normal.

Twelve of these 19 multiparas received pentobarbital sodium, gr. ivss-vi, and the other 7 women required neither analgesia nor anesthesia. In the first group, the normal sugar level averaged 84 mg., the labor average was 100.5 mg., a rise of 19.6 per cent. The postdelivery average level was 118 mg., or 40.5 per cent above the normal average.

Figures for the 7 women who had no medication of any sort show the following; average duration of labor of four hours. An average normal blood sugar of 89 mg.; a labor average of 116 mg., up 30 per cent and a postdelivery average of 128 mg., up 44.9 per cent above normal.

Combining our figures for all the cases, we find our average normal to be 87 mg. Labor average to be 107.6 mg., up 23.7 per cent. Postdelivery average of 120 mg., 38 per cent above normal.

Table I serves to illustrate more graphically the changes noted.

TABLE I

GROUPS	DURATION OF LABOR HR.	AVERAGE NORMAL BLOOD SUGAR	DURING LABOR		POSTDELIVERY	
			BLOOD SUGAR	% RISE	BLOOD SUGAR	% RISE
6 Primiparas (morphine and scopolamine)	18.5	87.5	111.0	26.8	115	31.4
12 Multiparas (nembutal)	10	84.0	100.5	19.6	118	40.5
7 Multiparas (no analgesia)	4	89.0	116.0	30.0	128	44.9
25 Combined	10.5	87.0	107.6	23.7	120	38.0

In only 3 patients, the blood sugar levels, during labor fell below predetermined normal figures. The drop was only 7 mg., or 8 per cent. Postdelivery figures on these 3 were 121 mg., or 40.7 per cent above normal.

In 5 cases after an average rise of 36.4 per cent in blood sugar during labor, there was a fall from 122 to 98 mg., but this last figure was still 9.6 per cent above "average normal."

The highest postdelivery sugar recorded (166 mg.) was by a para ii in labor for thirty-six hours. She delivered spontaneously a 5 pound premature baby and had a retained placenta. One patient had a mild post-partum hemorrhage with no effect on sugar figures.

SUMMARY

Average prenatal fasting sugar level proved to be 87 mg. The average rise during labor was 20.6 mg. or 23.7 per cent above normal. The highest was 151 mg. and the lowest 68 mg. These figures do not agree with those of Rowe and McManus[2] who found no rise until after the second stage. In the hour after delivery there was a further rise of 11.5 per cent above the labor average, to 120 mg., which was 38 per cent above normal.

CONCLUSIONS

There seems to be a fairly consistent rise in blood sugar levels during labor, and a further rise occurs in most cases within the hour after the termination of labor. Hyperglycemic figures were obtained in several patients with no stigmas of diabetes and glycosuria was not seen.

Dangerously low blood sugar levels were not seen either during or after the termination of labor.

It may be of interest to note that neither parity, nor type of delivery, nor use of analgesia or anesthesia seemed to influence the figures obtained.

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NON-EFFECT OF OVARIECTOMY DURING PREGNANCY IN THE RHESUS MONKEY

CARL G. HARTMAN, PH.D., BALTIMORE, MD.

(From the Department of Embryology, Carnegie Institution of Washington)

THE rôle of the corpus luteum in the production of progestational proliferation of the endometrium, that is, preparation for the nidation of the ovum, is now fully established.[1-6] How soon after nidation, however, the corpus luteum remains indispensable for the maintenance of pregnancy has been determined for only a few mammalian species. The pregnant rat, mouse or rabbit, for example, invariably aborts after castration, while the guinea pig, which has a long span of gestation, can spare its ovaries after the midperiod. In man, the matter is under dispute. From the clinical literature many cases can be cited in which abortion was seen to follow removal of the corpus luteum, while there remain positive cases in which castration did not interfere with pregnancy. Indeed, estrin as well as pregnandiol glucuronidate (degeneration product of progesterone)[7] is recoverable from the urine despite removal of the ovaries. One may infer from this that sooner or later the placenta takes over certain ovarian functions.

It is not the purpose of the present paper to discuss the clinical literature but only to present five experiments on the monkey for whatever of value they may possess toward a solution of the problem.

CONDITIONS IN THE MONKEY

In the monkey implantation occurs at the end of the ninth day following fertilization.[11] The gestation period approximates six lunar months (average 165 days).[8]

Certain events of interest to the present problem have been noted to occur soon after the third week. In the first place, anterior pituitary-like hormone (prolan), present in the urine from the seventeenth day on, disappears after the twenty-first day and does not reappear.[9] Second, about the 25th day the corpus luteum of pregnancy regresses somewhat and assumes a more compact structure,[10] in which

condition it remains for several months. Third, by the end of the fourth week, with the establishment of villi, the destruction by the trophoblast of proliferated uterine epithelium is over.[11] Finally, the female gradually loses all sex responsiveness.[12]

In view of these facts, most of all in view of the establishment of villi by the thirtieth day, one might expect this date to constitute a dead line, before which the corpus luteum is essential, after which it may be removed without disturbance to the implantation. This assumption finds confirmation in the last experiment cited below.

PROTOCOLS

MONKEY 469.—This old multipara weighed 7,870 gm. when she arrived on Aug. 14, 1936; 8,500 gm. later. Her menstrual cycles before conception, which occurred on Jan. 31 and Feb. 1, 1937, day 13 of cycle, were 30, 28, and 27 days in length. The placental sign began on February 18. Palpation from time to time showed a normal pregnancy in progress; the buttocks were maximally colored throughout pregnancy and lactation.[8]

On May 5, the ninety-fifth day of gestation, the left ovary containing the corpus luteum of pregnancy was removed. Serial sections of the ovary disclosed the corpus luteum in a good state of preservation.

On July 20, the one hundred seventy-first day of gestation, a normal male baby weighing 360 gm. was born. The mother ate the placenta; her pelvic ligaments were relaxed as normally despite the ovariectomy. The baby nursed well until September 20, when it was used in a crucial experiment.

Summary: Removing one ovary containing the corpus luteum on the ninety-fifth day of gestation, leaving the other ovary intact, in no recognizable manner affected the course of pregnancy, parturition, or lactation.

MONKEY 391.—This 6-kilo female was pregnant when she arrived on April 23, 1935. She gave birth to a 490 gm. male baby on June 22, which was removed two days later. On Oct. 17, 1936, the endometrium was excised in the hopes of finding a fourteen-day ovum, but fertilization had not taken place. The next bleeding occurred on November 19; the placental sign began on December 12. Conception occurred in the interval despite the contraceptive use of a small rubber sponge soaked in undiluted vinegar. Ovulation was estimated to have occurred on Nov. 28, 1936.

On Feb. 25, 1937, when the fetus was about 89 days old, the left ovary, containing the corpus luteum of pregnancy, was removed. Serial sections showed the corpus luteum to be in exactly the same condition as that of the preceding case (No. 469). On May 13 a 360 gm. male baby was born; the gestation lasted about 166 days, approximately the average for the rhesus monkey. Despite the fact that the mother was not in the best of health, pregnancy seemed perfectly normal. She took little interest in the baby, however, which was removed the next day and raised on a bottle. The mother died on June 7.

Summary: Complete castration on about the eighty-ninth day of gestation caused no abortion despite the poor physical condition of the mother, which delivered a viable baby at term.

MONKEY 457.—Mature female between 4,290 and 4,580 gm. in weight. After a twenty-five- and a twenty-six-day cycle she conceived and on Feb. 7, 1937, the endometrium was enucleated and an eleven-day ovum recovered. The right ovary containing the corpus luteum was also removed. Conception occurred again on Oct. 30 and 31, 1937, day 12 of the cycle; the placental bleeding began on November 16. On December 15, the forty-sixth day of gestation, the surviving ovary was removed. Palpation from time to time demonstrated the continuance of a normal pregnancy. By March 5, the one hundred twenty-sixth day of gestation the female had become considerably emaciated, due to tuberculosis as the autopsy later revealed; but the fetus seemed alive and the mother's buttocks red as usual. During the night of March 13 and 14, however, the one hundred thirty-fifth day of gestation, the animal died after first giving birth to a dead male fetus in a good state of preservation. The afterbirth was also delivered.

The hypophysis removed at autopsy showed the usual hypertrophy of pregnancy (at least a fourth larger than normal). There were no changes in this case attributable to lack of pregnancy hormones due to castration, the death of the fetus and of the mother being clearly a consequence of disease.

Summary: Complete castration on the forty-sixth day of gestation did not interrupt pregnancy in this tuberculous female which carried a baby to the one hundred thirty-fifth day and died immediately after delivery.

MONKEY 567.—A mature female weighing 4,710 gm. when she was received on Aug. 3, 1937. Conception ensued consequent upon a single mating on December 6 and 7, days 11 and 12 of the cycle. On Jan. 11, 1938, the thirty-fifth day of pregnancy, the left ovary containing the corpus luteum was removed. Examinations on January 25 and on February 9, indicated a pregnancy going on in normal fashion. On March 5 the uterus and embryo seemed normal but the sex skin several shades paler. On March 11 a bleeding set in and palpation disclosed a soft, mushy uterus. Pregnancy was clearly at an end. The animal was killed on March 14 in an advanced stage of pulmonary and abdominal tuberculosis. The pituitary showed the usual enlargement of pregnancy. The mammary acini were greatly dilated as in a secreting gland. Gestation had lasted but fifty-three days after ovariectomy.

Summary: Semicastration on the thirty-fifth day of pregnancy failed to precipitate abortion, which, however, occurred about fifty-three days later.

MONKEY 466.—A 4,430 gm. female had cycles of 29, 32, and 24 days, respectively, in the fall of 1936. On February 15 she furnished a 1-celled ovum and at this time the left ovary with fresh corpus luteum was removed. In April ovulation followed injection of extract of pregnant mare's serum (Gonadogen Upjohn). On October 25 a thirteen-day ovum was removed by hysterotomy. On December 4 and 5, days 12 and 13 of the menstrual cycle, she conceived again and on December 21 the placental sign appeared. On January 4, the thirty-first day of pregnancy, the surviving (right) ovary was removed. On January 10 the sex skin was several shades paler than normal but returned to a brilliant red after a few days, in which condition it continued. By March the female gave evidence of pulmonary tuberculosis (confirmed at autopsy), but pregnancy continued in perfectly normal fashion. Since a 140-day fetus was desired for a neurologic experiment and since the continuance of pregnancy without ovaries was sufficiently established by this time, the fetus was removed by cesarean section, after which the mother was killed and autopsied. The male fetus was normal as was also every other indicator of normal pregnancy: uterus, placenta, sex color, hypertrophied pituitary.

Summary: This tuberculous monkey despite complete castration on the thirty-first day of gestation, carried a normal, vigorous fetus to the one hundred fortieth day, when it was removed by cesarean section.

DISCUSSION

The results of five experiments, summarized in Table I, clearly show that, at least after the thirty-first day of gestation, the rhesus monkey can dispense with the corpus luteum. This conclusion is justified even though the third and fourth experiments (No. 457 and 567) are thrown

TABLE I. SUMMARY OF CASTRATION EXPERIMENTS

ANIMAL NO.	DAY OF PREGNANCY OPERATED	ONE OVARY OR BOTH REMOVED	RESULT
469	95	One	Normal delivery at term
391	89	Both	Normal delivery at term
457	46	Both	Premature delivery on 135th day; death of mother
567	35	One	Resorption after 88th day
466	31	Both	Normal pregnancy, cesarean section on 140th day

out. This seems hardly necessary, however, for both pregnancies continued two to three months after castration, that is, through the more vulnerable period. The animals achieved this (as did also No. 466) despite general physical debility due to disease.

Abortions are common in the monkey even without surgical interference.[8] Thus, at the time the first two experiments were under way the Carnegie Colony possessed two other females at about the same stage of pregnancy. These were left unoperated, since newborn babies were desired. These two unoperated "controls" aborted, the two castrated individuals went to term!

Except in the case of 567, all females gave ample evidence of endocrine sufficiency, namely in the sex skin of maximal redness; in a full and turgid uterus; in normal, growing mammary glands; in the hypertrophied pituitaries; in the inactive vaginal mucosa,[13] and in the relaxation of pelvic joints.

SUMMARY

A monkey castrated on the thirty-first day of gestation furnished on the one hundred fortieth day a vigorous baby removed by cesarean section. Four additional experiments help to demonstrate the dispensability of the corpus luteum in the monkey after the first month of pregnancy.

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The relation between chronic cervicitis and bladder irritability is emphasized. Frequency of urination of this type is associated with noninfected urine and a normal bladder. The authors believe that it is due to reflex stimulation through the parasympathetic nerves to the bladder. In a high proportion of cases relief is obtained by dilatation and cauterization of the cervix with the electric cautery. In intractable cases, injection of the pericervical nerve plexus, particularly in the region of the bladder base, gives immediate relief without interfering with bladder function. This relief is often transient.

CARL P. HUBER

THE RELATION BETWEEN HYDATID MOLES, RELATIVE ISCHEMIA OF THE GRAVID UTERUS, AND THE PLACENTAL ORIGIN OF ECLAMPSIA*

ERNEST W. PAGE, M.D., BERKELEY, CALIF.

(From the Department of Obstetrics and Gynecology, University of Southern California and the Los Angeles County Hospital.)

ANY working hypothesis applied to the origin of the toxemia syndrome in late pregnancy must be able to correlate in a satisfactory manner the known facts pertaining to the occurrence of eclampsia. The writer wishes to point out very briefly a working hypothesis which has not been discussed before, but which would seem to deserve serious consideration. Attention was first directed to this theory by an inquiry into the relative frequency with which hypertension and albuminuria accompany hydatidiform moles, and for that reason the results of the analysis are presented below.

Individual case reports of eclampsia accompanying hydatid moles have been made from time to time[1, 2] but it has not been known whether such tumors statistically predispose to the development of the toxemia syndrome. During a nine-year period from 1928 to 1937 inclusive, thirty women with hydatid moles were treated at the Los Angeles County Hospital. Ten of these women developed pre-eclamptic toxemia, as evidenced by a sustained blood pressure over 140 systolic and 90 diastolic, the presence of albumin in the urine and the development of the usual subjective symptoms of late toxemia. Three of these ten cases were graded as severe pre-eclampsia, while the remainder were mild toxemias.

Such facts are of greater significance when the duration of the pregnancies is taken into consideration. The cases were arbitrarily divided into early stages (less than four months' amenorrhea, or a tumor below the level of the umbilicus), and late stages (from four to seven months' amenorrhea, or a tumor above the level of the umbilicus). Of the 16 early cases, there were no instances of pre-eclamptic toxemia. All ten of the toxemias were found among the 14 hydatid moles which were of four to seven months' duration, an incidence of 71 per cent. Using the same criteria, it was found that among 3,850 consecutive deliveries at the same hospital there were 346 women (9 per cent) who developed the toxemia syndrome, almost always during the last trimester. In this short series, therefore, the incidence of pre-eclamptic toxemia in women with hydatidiform moles in the middle trimester was almost eight times as high as the incidence of toxemia in late pregnancy.

While such facts are subject to numerous interpretations, it seems reasonable to assume that the more rapid growth of the vesicular

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placenta demands a greater blood supply than does a normal placenta of the same age. To revert for a moment to teleologic reasoning, if the placenta (which appears to be a ruthless parasitic organ existing solely for the maintenance and protection of the fetus, perhaps too often to the disregard of the maternal organism) should be unable to obtain a sufficient maternal circulation for its demands, it might be capable of increasing this supply by raising the systemic blood pressure. Since there are no nervous connections by which the placenta could accomplish this, such a postulate necessitates the concept of a "placental pressor substance" capable of being produced by all chorionic tissue in response to a relative ischemia. Recent contributions[3] in the field of experimental renal hypertension have shown that the kidney is able to effect hypertension by a similar mechanism, and to the same stimulus of reduced blood flow. Since the placenta is the excretory organ of the fetus, it is not illogical to consider that it may also possess a similar secretory function. While the transference of blood from patients with eclampsia to normal pregnant women[4] has not demonstrated any circulating pressor substance, the method does not give conclusive proof of its absence, and furthermore, the same method has yielded negative results in the case of experimental hypertension[5] where a circulating pressor substance must exist.

That the normal placenta is capable of producing pressor substances is indicated by preliminary assays. The rather crude extracts which I have prepared by extracting acetone-desiccated powders of fresh placental mash with Locke's solution for twenty-four hours were kindly tested by Dr. Eric Ogden on unanesthetized dogs and were found to possess marked pressor activity in relatively small doses. Depressor substances are also present in varying amounts along with many other substances, and considerable purification with repeated assays must be accomplished before the chemical nature of the pressor fraction is understood. Using the same method of extraction, Pickering and Prinzmetal[6] were able to find such pressor activity only in kidney cortex, but did not make tests on placental material.[7] There is also some evidence to indicate that the "placental pressor substance" may be capable of producing marked injury to capillaries.

Many of the known clinical facts regarding eclampsia may be correlated with such a postulate. A relative ischemia of the gravid uterus may, of course, result from an increased demand for blood supply, an actual decrease of maternal blood supply, or a failure of the developing uterine circulation to keep pace with the increasing demand. Multiple pregnancy or advanced hydatid mole would presumably create a greater demand and are known to be predisposing causes of eclampsia. The intrauterine death of a fetus would obviously result in a decreased placental function, and commonly results in a subsidence of the maternal hypertension.

It is well known that toxemias occur more often in primiparas, a fact which few of the present theories of eclampsia can account for. Is it not conceivable that a primigravid uterus is less capable of develop-

ing a high degree of vascularity than a uterus which has once developed a tremendous vascular bed in a previous pregnancy? If this were so, then an infantile type of uterus would further predispose to the development of a toxemia. Infantile genitalia are frequently associated with a constitutional type of woman presenting hypothyroid-hypopituitary-hypogonadal syndromes, an endocrine type known to be predisposed to the development of eclampsia.[8]

Quite obviously, the fetal demands increase with the duration of pregnancy, and similarly the incidence of toxemias increases with the duration of pregnancy. The additional ischemia resulting from uterine contractions (or from overdistention as in hydramnios) may account for the frequent onset of eclampsia during labor. The placental infarcts so commonly associated with toxemias may be manifestations of this inadequate maternal circulation. The rapid decrease in the frequency of eclampsia with each post-partum day may be similar to the rate of excretion of such a vascular toxin or to the rate of the reparative processes taking place in the liver, kidneys, brain, and other viscera. The existence of a case in which the onset of the entire toxemia syndrome occurred a week or more after delivery would be strong evidence against such a hypothesis, but a proved case of this sort is not on record.

Based on the assumption that the more adequate collateral blood supply to the pelvic organs in the lower mammals may prevent them from developing eclampsia spontaneously, experiments are under way in which the blood supply to the gravid uteri of various mammals is artificially limited. These and similar experiments should adequately test the validity of the theory. It is hoped that such suggestions may be of assistance to other investigators interested in the pathologic physiology of eclampsia.

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The author emphasizes the difficulties in making an exact diagnosis of hydatid mole before a part of the mole is expelled or removed. He therefore recommends the procedure of Albino, a puncture of the uterus through the abdominal wall. This procedure is without danger. In cases of normal pregnancy only normal liquor amnii will be obtained and no harm done. The pregnancy will continue. In the case of a mole, no fluid will be obtained even after repeated punctures.

J. P. GREENHILL.

BARTHOLINITIS AND SKENEITIS DUE TO TRICHOMONAS VAGINALIS

HERMAN A. SHELANSKI, M.A., AND SAUL P. SAVITZ, M.D.,
PHILADELPHIA, PA.

(From the Department of Zoology, University of Pennsylvania, and Philadelphia General Hospital.)

FOR many years *Trichomonas vaginalis* has been recognized as commonly occurring in vaginal discharge. More recently it has been observed in the male urethra and prostate, and the possibility has been discussed of the presence of the organism in the blood, tubes, ovarian cysts, and urine.[1]

It has also been suggested that *Trichomonas vaginalis* is capable of producing urethral discharge and bartholinitis.[2] In the investigation reported here, the organism has been demonstrated in Bartholin's and Skene's glands, thus suggesting a new possibility in transmission of the infestation and identifying as a pathologic entity the so-called nonspecific or nongonorrheal bartholinitis and skeneitis. Despite the common belief that bartholinitis and skeneitis are most frequently due to Neisseria infection, it has been conclusively shown in this study that the inflammation of these glands may be due to *Trichomonas vaginalis* and its symbiotic bacteria, without the presence of any of the Neisseria group.

During previous investigations of *Trichomonas vaginalis* vaginitis, edematous vulvas were noticed in the few patients who did not respond promptly to treatment. These recurrent cases were recalled to the clinic, and trichomonads were isolated from the Bartholin glands. Treatment of these glands as described below relieved the patients of the bartholinitis and subsequent insufflation of the vaginal tract controlled the vaginitis. These cases were further studied and the following information was obtained.

DIAGNOSIS

The diagnosis of the vaginal infestation has been discussed both from the laboratory and clinical aspects by many workers. The diagnosis of cases in which *Trichomonas vaginalis* is present in the glands of Bartholin or Skene is equally simple. With the patient in the lithotomy position an unlubricated speculum is inserted into the vagina. A vaginal smear, taken on a sterile applicator, is diluted with several cubic centimeters of normal saline or modified Ringer's solution,[3] and a drop of the dilution is examined under the high dry power of the microscope for trichomonas. In the cases studied in this report all were positive for vaginal trichomoniasis. The vagina and the entire external genitalia are then cleansed with an aluminum hydroxide gel and kaolin suspension, which has been found very efficient for this purpose. Then the Bartholin or Skene glands are palpated so that some of the glandular secretion is expressed. This

secretion may either be diluted with several cubic centimeters of saline in a test tube, as is the vaginal smear, or it may be placed directly on a slide and there diluted with saline. Microscopic examination is made the same way as for the vaginal smear. The methods of preparing stained specimens of cultures have been described previously.[4]

The clinical picture is typical and in most cases resembles gonorrheal bartholinitis or skeneitis. However, some of the cases show only a slight swelling of the labia and are not quite as inflamed or edematous as are the gonorrheal cases. Patients may have itching and burning of the external genitalia without the parasite being present in the vaginal secretion, with the Bartholin or Skene glands the only foci of infestation. Itching of the external genitalia, in most cases unilateral, may be considered suggestive of *Trichomonas bartholinitis* and *skeneitis.*

TREATMENT

The patients are prepared for treatment by cleansing the vaginal tract, cervix, and fornices with the aluminum hydroxide gel and kaolin suspension, in order to remove all of the mucoid material and débris. Special attention is given to the plug of mucus usually resistantly present in the cervical canal. This plug of mucus is removed by means of a sterile applicator, moistened with the suspension, which is inserted in the os and rotated between the thumb and index finger until the plug is coagulated and may be removed. In cases where the plug of mucus is closely adherent, the removal of this plug causes slight bleeding.

The infested glands are then treated by injection with 1 c.c. of 1 per cent aqueous solution of silver picrate.* As is shown in Table I, the glands in 9 patients were

TABLE I*

CASE	DURATION OF DISCHARGE AND SYMPTOMS	RECURRENCES WHILE UNDER TREATMENT FOR VAGINITIS	TRICHOMONAS VAGINALIS				NEISSERIA GONORRHEA	NUMBER OF TREATMENTS
			BARTHOLIN		SKENE	VAGINA		
			LEFT	RIGHT				
1	2 yr.	3	+	+	−	+	−	4
2	1 yr.	5	+	+	−	+	−	2
3	2½ yr.	5	+	+	+	+	+	2
4	6 mo.	3	−	+	−	+	−	2
5	3 yr.	6	−	+	−	+	−	Excised
6	2 yr.	1	+	−	+	+	−	2
7	3 yr.	2	−	+	+	+	−	2
8	4 mo.	0	−	+	+	+	−	2
9	8 yr.	3	+	+	−	+	−	5
10	1 yr.	2	−	+	−	+	−	2
11	8 mo.	3	+	+	−	+	+	Excised

*Plus and minus signs indicate that diagnosis was positive or negative in smear and culture.

injected, while in 2 patients they were excised. Two injections cleared the infestation in 7 patients. One patient required four injections and another case 5. In cases where the organisms were present in but one of the Bartholin glands, both glands were injected as a precautionary measure. Injection of the glands was followed by the silver picrate treatment for vaginal trichomoniasis. This consists of an insufflation with 5 gm. of 1 per cent silver picrate-kaolin powder, followed by a course of 6 silver picrate suppositories to be used at home by the patient. This procedure is repeated one week later.[5] In the first 3 of the 11 patients treated the

*Supplied through the courtesy of John Wyeth & Brother, Incorporated, Philadelphia.

infestation of the glands was not suspected until after several recurrences of vaginal symptoms, when the inflamed and edematous appearance of the Bartholin glands suggested that site as a focus of repeated infestation of the vagina. The other patients showing Bartholin gland symptoms were treated at the time of the initial vaginal treatment.

RESULTS

Before silver picrate treatment, the duration of the discharge and symptoms had varied from four months to eight years in the cases studied. The number of recurrences also varied. In some cases the number of recurrences may have been due to the duration of time the infestation was present (Case 5). However, in some cases the number of recurrences may have been due to the virulence of the strain of trichomonas present (Case 2).

All of the cases were positive for *Trichomonas vaginalis* in the vaginal tract. In 5 patients (Cases 1, 2, 3, 9, and 11) the trichomonads were found in both Bartholin glands; in one patient (Case 6) they were found only in the left gland, while in 5 cases (Cases 4, 5, 6, 8, and 10) the parasites were found only in the right gland. Four patients (Cases 3, 6, 7, and 8) were found to have trichomonas present in Skene's gland. Two patients (Cases 3 and 11) had in addition to *Trichomonas vaginalis* a Neisseria gonorrhea infection.

The Bartholin glands were excised in 2 patients (Cases 5 and 11), while in the other 9 patients they were injected with silver picrate. Seven patients (Cases 2, 3, 4, 6, 7, 8, and 10) were relieved of the bartholinitis with 2 injections and 1 patient (Case 1) with 4 injections; while 1 patient (Case 9) required 5 injections. Injections into the Bartholin and Skene ducts were given one week apart. Each patient was observed for a period of four months after the last treatment, and at the end of that time all were found to be negative. In none of these patients was there observed any nephritis, dermatitis, or other untoward reaction to silver picrate.

DISCUSSION

One of the outstanding obstacles in treating trichomonas infestations in the vaginal tract is reinfestation, for which several explanations have been suggested such as:

1. Reinfestation from the male.
2. Recurrence due to the organisms in the cervical plug of mucus.
3. Infestation of the glands of Bartholin and Skene.
4. Contaminated plumbing fixtures on which organisms will remain viable for as long as twenty-four hours if kept moist.
5. Reinfestation from the bladder or urethra.

Silver picrate has been used in the treatment of *Trichomonas vaginalis*[4-6] and has been shown to be highly germicidal to this organism in vitro.[7] Thus its use in *Trichomonas bartholinitis* and *skeneitis* is an extension of these former investigations.

CONCLUSIONS

1. *Trichomonas vaginalis* has been demonstrated in Bartholin and Skene's glands, and is a specific factor in producing bartholinitis and skeneitis.

2. The presence of *Trichomonas vaginalis* in these glands demonstrates that they act as foci of infestation. These glands, therefore, are one source of constant reinfestation in recurrent cases of *Trichomonas vaginalis* vaginitis.

3. Injection of the glands with 1 per cent solution of silver picrate has been found to be a satisfactory treatment for this infestation.

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LITHOPEDION DEVELOPED FROM EXTRAUTERINE GESTATION IN INTRAUTERINE AND EXTRAUTERINE PREGNANCY

Albert Mathieu, M.D., F.A.C.S., Portland, Ore.

(From the Department of Gynecology, University of Oregon Medical School, and the Gynecologic Service, Multnomah Hospital)

A LITHOPEDION (calcified fetus) is on rare occasions discovered during the performance of an abdominal operation, at necropsy, or by roentgenography. It may be retained in the abdominal cavity for a long period of time without harm to the mother or injury to subsequent pregnancies.

There are in the literature a number of excellent papers on the pathologic changes of this anomaly, and there are a few exhaustive reviews of the recorded cases. In 1933 Bland and others[3] reported a case and summarized 13 others which they had collected from the literature. Adding these 14 cases to the 183 assembled by Masson and Simon[18] in 1928, they estimated the aggregate of reported lithopedions at 197. In a review of the literature, from the point at which Bland and others stopped to 1937, we found 31 additional cases. These and the one herein reported bring the total number of recorded cases to 229.

Of interest in our collection of 31 cases is the fact that in 22 the lithopedion was successfully removed. As far as we could determine, there was only one death following operation. This patient[28] was a 64-year-old negress who had carried a calcified eight months' fetus as an abdominal tumor for forty years. In 3[17, 21, 25] of the remaining 8 patients no operation was performed; in 3 others[13, 19, 23] the lithopedion was not discovered until necropsy was done after death from some other condition; and finally, in 2 instances[24, 30] we had no details about the cases beyond the notation that the presence of a lithopedion had been determined. In 8 instances diagnosis was made by means of the roentgen ray.

The ages of the patients varied from 30 years[31] to 100 years,[17] and 3 patients[13, 19, 23] were in the late seventies. The period during which the lithopedion was retained varied greatly in the different cases, from four years[16] to sixty years,[17] although in the majority of the cases in this series the lithopedion was carried for less than twenty-five years. The development of the fetus, while not recorded in all cases, also showed considerable variation.

Among the cases of more than usual interest is that reported by Umnova.[29] His patient had a calcified mass removed from either side of the abdomen. Roentgenograms showed that each mass contained a lithopedion, one of two or three months' development and eleven years' duration, the other of six months' development and nine years' duration. Varchavsky and Elenevskaja[31] reported the case of a woman

who was operated upon and found to have had a bilateral tubal pregnancy with transformation into a lithopedion on one side and into a secondary abdominal pregnancy carried to term on the other side. In one case reported by Jonas[15] operation revealed an old calcified fetus in the right ovary and a smaller, more recent pregnancy attached solely to the omentum. Timko[27] and Figueroa Casas[8] each reported the removal of a lithokelyphopedion.

COMBINED INTRAUTERINE AND EXTRAUTERINE PREGNANCY

Combined intrauterine and extrauterine pregnancy (simultaneous existence of an intrauterine and extrauterine embryo) is almost as rare as lithopedion formation. While a number of reviews of the literature of this condition have been published, there is a slight variation in the computations of the different reports. The largest collection of cases was made by Neugebauer[71] who, according to Novak, assembled 244 cases from the earliest records to the year 1913. Continuing from 1913 to 1926, Novak[72] found 32 others (30 in the original paper and two postscript cases), and added two he had observed. In 1928 Stein[81] published his collection of 36 cases, including one of his own. But 17 cases he assembled were also included in Novak's group. Deducting the 17 cases duplicated by both Novak and Stein, and adding the remaining cases to those of Neugebauer, the total number of recorded cases to 1928 was 297. Gemmell and Murray,[53] in a very exhaustive review, say: "Novak, in 1926, reviewed recent cases and stated that, with those already published, the total on record was then 276. The present paper, however, while taking note of papers published up to the end of 1931, in fact only deals with 217 cases, 213 from the literature, one read at the North of England Obstetrical and Gynaecological Society, April, 1932, one reported to the Royal Society of Medicine, April, 1932, and our own two cases. Examination of the literature has made it very obvious that numerous cases have been included in reviews which were not really eligible, as for instance, twin pregnancy in a fallopian tube or simultaneous pregnancy in two horns of a bicornuate uterus, both embryos being later expelled per vias naturales. We have, therefore, limited our survey and statement of literature to cases in which we have personally studied the original article or an abstract of it. A group of 22 cases, mentioned in a later paragraph, is also excluded from the total as it deals with intrauterine and extrauterine pregnancies which were not truly simultaneous."

Because our study overlaps that of Gemmell and Murray, we have not counted cases from 1928 through 1931 included by them. We have, however, added 19 cases between those years that we could not find in their study. Our study through 1936 has added 57 cases,* including the case we report. Adding these to the 217 assembled by Gemmell and Murray, we obtain an aggregate of 274 recorded cases to the end of 1936.

It is interesting to note that in 24 of the cases we assembled, operation for the ectopic pregnancy did not interrupt the coexisting intrauterine pregnancy which in the majority of the cases terminated in normal delivery. In 3 of these cases[36, 41, 46] the intrauterine pregnancy was carried to term in spite of the grave internal hemorrhage which accompanied the operation for the ectopic pregnancy. In 25 instances, however, the concurrent intrauterine pregnancy ended in abortion, before laparotomy in 19 cases and after laparotomy in six. There was one set of intrauterine twins[80] in this group. One patient[40] died half an hour after operation for the ruptured ectopic gestation. In 2 instances[42, 68] laparotomy was done for the tubal pregnancy, but no mention was made concerning the termination of the coexisting intrauterine gestation. And in 4 cases[34, 37, 60, 64] we had no information beyond the fact that there was a combined intrauterine and extrauterine pregnancy.

*In this review, as in that of the lithopedions, it was noted that several authors mentioned cases observed by others, but did not give sufficient details or adequate references. Such cited cases were not counted. In a few instances where the cross reference could be checked, it was found that the cases had already been included in previous studies. Although we have used every available resource in our attempt to include every case, we have probably missed some.

In most of the cases the tube had already ruptured before the patient was operated upon. In a few instances[43, 47, 50, 62, 78, 84] the associated pregnancy, either intrauterine or extrauterine, was not discovered until operation was performed. Schubert[77] reported an ovarian pregnancy combined with an intrauterine pregnancy. A roentgenogram of the abdominal tumor, taken six months after the spontaneous premature delivery of a stillborn child, revealed the extrauterine fetus which was found at subsequent operation to be papyraceous and of four months' development. In one of his cases, Sunde[82] reported the delivery by cesarean section of an intrauterine infant that lived eight hours and of an extrauterine infant that lived five minutes. Weintraub[86] reported the vaginal delivery of a living, premature infant followed by the delivery of a coexisting living, deformed extrauterine child.

LITHOPEDION FOLLOWING COMBINED PREGNANCY

Combined intrauterine and extrauterine pregnancy in which the extrauterine gestation develops into a lithopedion must be extremely rare. In our search through the literature we were able to find only one case with such a sequence. It was reported by Hayward[12] in 1934.

The patient in this case was married at 16 years of age, was divorced six years later, and then remained single. Her menstrual history was normal, and was interrupted only during pregnancy and lactation which began two weeks after her marriage. After the sixth week of this pregnancy, the patient had a sudden pain in the left lower quadrant accompanied by symptoms of shock. Because of the unusually large abdomen, twins were suspected. Labor was prolonged and difficult, and resulted in the birth of only one child. The abdomen remained large after delivery, and did not regain its normal contour. One month later a diagnosis of uterine or ovarian tumor was made, and a year later the patient was told she had a uterine tumor. Because she was having no discomfort, she did not have the operation which was then advised. Twenty-six years later, when she was 43 years old, she was operated upon because of a tentative diagnosis of acute appendicitis and calcified fibromyomatous uterus. And it was during this operation that the lithopedion was found.

The case we wish to report is of the same kind. That is, we believe that our case has the criteria necessary to label it a lithopedion developed from the extrauterine gestation in a combined intrauterine and extrauterine pregnancy. As far as we are able to determine, this is the second case of this type to be reported.

CASE REPORT

Mrs. A. A., white, aged 47, entered Multnomah Hospital, Nov. 19, 1934, complaining of painful swelling of the left labia majora. The important facts in her past history were as follows: She was married in 1906. In 1908 she became pregnant for the first and only time, missing her menstrual periods in January, February, March, and April of that year. One morning while lifting, she had "labor pains" which radiated over the entire lower abdomen at fifteen-minute intervals. Eventually she passed a fetus which she saw and which her doctor said was of four months' development. Following the miscarriage she had chills and fever, and had to remain in bed for about two weeks. The doctor who attended her during this miscarriage has since died. The patient's mother, however, verified these facts.

Physical examination at the time the patient entered the hospital was negative except that pelvic examination revealed an infected Bartholin's gland cyst in the left labia and a mass, which was hard and movable, in the left lower pelvis. However, the pelvic examination was unsatisfactory because of the tenderness in the region of Bartholin's gland. The abscessed cyst was incised. Two weeks later, when the wound in Bartholin's gland had healed, another pelvic examination was made. At this examination it was found that the mass in the left lower quadrant

was movable, extremely hard, somewhat irregular in contour, and about 8 cm. in diameter. It was thought to be either a calcified ovary or an osseous formation in a dermoid cyst.

A roentgenogram of the pelvis (Fig. 1) showed a calcareous mass in the pelvis. The structures in this mass suggested a developed fetus, showing skull, extremities, and curved vertebral column with ribs. A diagnosis of lithopedion was made.

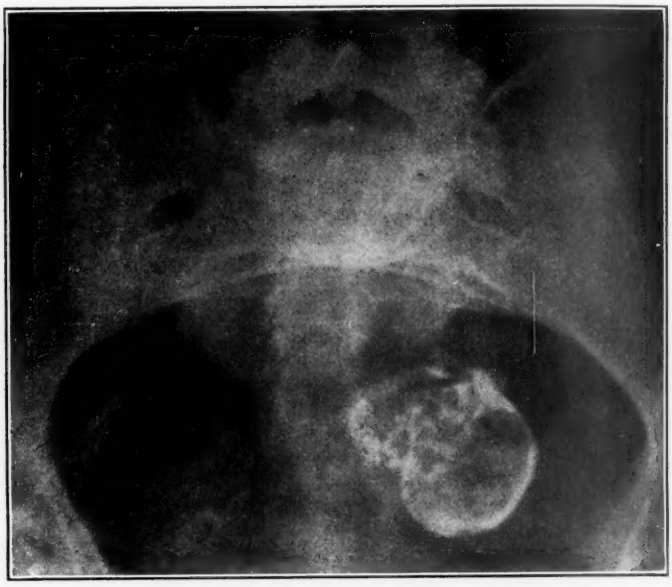

Fig. 1.—Roentgenogram showing lithopedion in the pelvis.

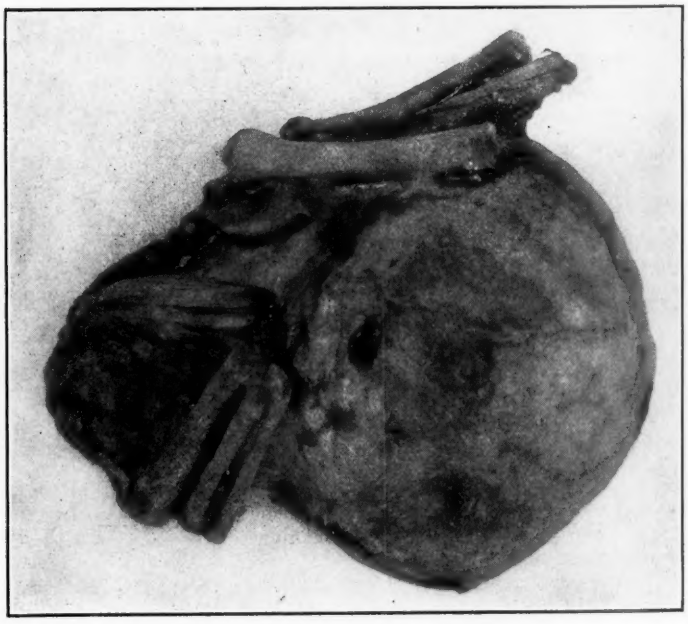

Fig. 2.—Lateral view of lithopedion.

On Dec. 7, 1934, the patient was operated upon. The abdomen was opened between the umbilicus and the symphysis. After liberating the omentum, which was adherent deep down in the pelvis behind the uterus, a calcified fetal mass was found. Its superior surface was covered by the omentum, and it was held in the pelvis by fine, cobweblike adhesions. It was, however, movable from side to side. The adhesions were broken down with the finger, and the lithopedion was easily delivered. The omentum, which was still attached to the fetal mass, was wiped off with gauze. Examination of the pelvis revealed a small fibroid on the anterior wall of the uterus. The fundus of the uterus was normal in size and position. The right ovary was normal. The right tube was also normal except for a small nodule in the isthmus. The left tube could be traced plainly from the uterus for a distance of about 3 cm., then it ended abruptly and the distal portion, with its fimbriated end, was plainly visible, completely separated from its proximal attachment and adherent to the peritoneum in the region of the infundibulopelvic ligament. When the ectopic pregnancy had ruptured, there had been a complete rupture of the tube with a separation of the segment. Further examination of the pelvis revealed a small long bone of the fetus attached to the peritoneal surface of the posterior pelvic wall. This also was removed. The patient made an uneventful recovery.

The lithopedion (Fig. 2) weighed 37 gm. It measured 6.5 by 5.75 by 3 cm. The biparietal diameters were 3 cm. and the occipitofrontal diameters 3.75 cm.

SUMMARY

1. The literature on lithopedions has been reviewed from 1932 to 1937. Thirty-one cases were found in this study. These added to the one herein reported make an aggregate of 229 reported cases to 1937.

2. A review has also been made of the literature on combined intrauterine and extrauterine pregnancy. From 1928 through 1936, 56 cases were found which, with the one now being reported, bring the total number of recorded cases to 274.

3. There is in the literature apparently only one other case of the type reported here, a lithopedion developed from the extrauterine gestation in a combined intrauterine and extrauterine pregnancy.

4. The lithopedion in the case reported at this time was discovered by roentgen ray. All evidence at hand tends to prove that the lithopedion had developed from the extrauterine gestation in a combined pregnancy, and that it had remained in the abdomen for a period of twenty-six years.

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III. Lithopedion Following Combined Pregnancy

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415 Stevens Building

TUBAL PREGNANCY WITH TUBERCULOUS SALPINGITIS

CHARLES SUMMERS STEVENSON, M.D., AND LAWRENCE R. WHARTON, M.D.
BALTIMORE, MD.

(From the Department of Gynecology of the Johns Hopkins Hospital and University)

A PERUSAL of the literature reveals that eight cases of coincidental tuberculous salpingitis and tubal pregnancy have been reported. In each the condition has been found at operation and established by histopathologic study. The purpose of this paper is to present a new case which is apparently the first proved case to be reported from the English-speaking world.

In the forty-seven years the Gynecological Pathology Laboratory has been in existence at the Johns Hopkins Hospital, we have had 402 cases of tuberculous salpingitis and 516 of tubal pregnancy. The case reported herein is the first in our laboratory to combine these two conditions.

The great infrequency of pregnancy in genital tract tuberculosis is in part due to the blocking off of the lumina of the tubes, both to ascending spermatozoa and descending ova. It is also due to the facts that the ova do not receive adequate nutrition from the diseased mucosa of the tube while passing down it and that the fertilized ova generally cannot become successfully imbedded in the diseased endometrium if and when they reach the uterine cavity alive (tuberculous endometritis is found in about 85 per cent of the cases of tuberculous salpingitis in our laboratory). Sterility, as is well known, is one of the symptoms of genital tract tuberculosis. A study[1] of the ovaries from women dying of pulmonary tuberculosis has shown that a high percentage of the primordial follicles are obliterated, which thus accounts for some degree of the sterility. However, in some cases,[2, 3] where the presence of tuberculous endometritis has been established by several curettements, the disease has later apparently cleared up and the women have had normal pregnancies and deliveries. The healing of the tuberculous endometritis in these cases is due both to its removal by curettement and to the regular menstrual desquamation[4] of the areas of normal endometrium where some of the tuberculous portions are shed with it. There is no opportunity for similar healing in tubal tuberculosis.

In tuberculous endosalpingitis, except where the infection is very extensive and pursues a rapid course with marked caseation, necrosis, and slough, the lumen generally tends to remain open to some slight degree, at least in the early stages. Many tubes show the familiar bulging of the ampullar portion with the contracted but patent abdominal ostium and free fimbriae giving the so-called "potato sack" appearance. Even in some cases where there is extensive caseation, the ostium and even the entire lumen may remain open. The lumen obstruction, when present, is usually found in the cornual portion of the tube and may be manifested chiefly by a tuberculous salpingitis isthmica nodosa. With healing there is scarring and thickening of the walls of the tube. As is well known, the mucosa is the original site of infection in the tube when the tubercle bacilli are blood-borne, and the spread takes place from the mucosa to the muscularis and, in severe cases, to the serosa. Histologically there are epithelioid tubercles with their Langhans' giant cells in the mucosal stroma. Around them there is an infiltration of lymphocytes. The adjacent columnar epithelium lining the lumen may show necrosis, or more usually hyperactivity with hyperplasia into several layers in depth, thus simulating the so-called "squamous metaplasia."

As some healing takes place the tips of the mucosal folds characteristically become adherent to each other and to neighboring adherent folds with the resultant

formation of many pseudoglandular epithelium-lined spaces of various sizes and shapes. Thus many "false passages" and "blind alleys" are created. In the cases of low-grade tuberculous salpingitis the healing may apparently go on at a rate equal to the spread of the infection, and many sections in our laboratory show extensive scarring of the serosal mucosa with only an occasional active tubercle. With several sections through one tuberculous tube widely differing degrees of the infection can be found, indicating that the tuberculosis may be more or less patchy in distribution. Thus, in a tube where there is slight tuberculosis of only low activity, the lumen may be open enough to allow the ascending passage of spermatozoa, while the many traps in the mucosal folds are likely to catch the descending fertilized ovum. If the mucosa lining the "trap" is diseased or scarred, the chances are that implantation cannot take place and the fertilized ovum will die. However, there is an apparent rare chance that the ovum might be caught between two mucosal folds in which the infection, for practical purposes, has cleared up. The implantation may then take place and the ovum may live and grow. The trophoblast may erode and extend through the mucosa, and since no decidua of practical importance is usually formed in the tube, the muscularis may be rapidly invaded. With the development and growth of the embryo, the expanding fetal sac becomes centralized in the lumen and continues to grow until the tube and sac rupture or the fetus dies from other causes. As a general rule, the less scarring there is in the tube wall, the greater is its elasticity and the longer and larger the fetus may grow before rupture. Since there is usually more scarring in the wall following a tuberculous infection than following a gonococcal one, earlier rupture or abortion of the tubal pregnancy will probably occur when the salpingitis is tuberculous.

* * * * *

The following is the clinical and pathologic report of a case of simultaneous tubal pregnancy and tuberculous salpingitis:

J. H. H. (Unit 77510), aged 37, married eleven years, no pregnancies. Admitted to the Johns Hopkins Hospital Feb. 12, 1937. Discharged March 5, 1937. Complaint: abdominal pain; vaginal bleeding. Family history: negative. Past history: the patient never had rugged health. Through childhood and adolescence she was so frail that her father, a physician, suspected that she had an occult form of tuberculosis, although he could never demonstrate it. She was married at the age of 26, and never became pregnant although she did not use any contraceptive measures. No serious illnesses, but always lacked strength and endurance. A highly educated woman, she has recently been working for a Ph.D. degree, but has never been able to work through the whole day. She has had to rest for an hour or two every afternoon since adolescence.

No significant or constant local discomforts. She has had mild attacks of cystitis in the last two years, due to *Staphylococcus albus* and colon bacilli. Had an appendectomy in 1921 at another hospital for chronic appendicitis, and a tonsillectomy was done in 1922.

Menstruation began at thirteen years, usual duration four to five days, with normal flow, slight pain, and no intermenstrual bleeding. The cycle has been irregular, her menses occurring every four to seven weeks. There has been frequent amenorrhea for periods of two to three months.

In this case the past history is particularly significant in that she was suspected of having tuberculosis in early life, but this was not revealed until she developed a tubal pregnancy. One of us (L. R. W.) observed this patient repeatedly during the two years preceding the operation and never suspected tuberculosis. No explanation could be found for the lack of resistance, the recurring cystitis, leucorrhea, amenorrhea and the sterility. Repeated pelvic examinations were negative. The remarkable improvement in health, gain in strength and physical endurance since the operation two years ago lead us to wonder whether this patient may not have had a latent tuberculosis of the Fallopian tubes and endometrium for many years.

Present Illness: On Dec. 13, 1936 (two months before the operation), she began to have a continuous spotty vaginal bleeding. This continued up until operation

except for a period of two weeks in January, 1937. The "menstrual" bleeding which began December 13 was thirteen days late, but this was not unusual. It lasted about seven days, after which there was only a slight daily spotting. One of us (L. R. W.) examined the patient December 29. At this time the cervix was hard, the uterus small, a small myoma was discovered, and the left adnexa were found to be enlarged to about 4 cm. in diameter. The enlargement was attributed to a corpus luteum cyst, which was the diagnosis at this time. A few days after this examination the bleeding stopped and the patient went South for a rest. There was no discharge whatever from January 8 until January 17, when the bloody spotting returned and lasted until January 23, at which time it became so definite that the patient thought she was menstruating. The flow was not as profuse as normal and lasted eleven days. During January the patient had felt well and had been free from pain.

Another pelvic examination was made on Feb. 5, 1937, when the findings were a little more definite than on Dec. 29, 1936. The uterus was still small, hard, freely movable and insensitive. At the left cornu there was some irregularity and there was a round mass low in the left fornix which was thought to be a physiologic cyst of the left ovary.

Seven days later, February 12, the patient was suddenly seized with general abdominal pain, most severe in the pelvic region. Vomiting developed in about an hour. At that time there was abdominal rigidity. A mass could still be felt in the left fornix on pelvic examination. The preoperative diagnosis was intra-abdominal hemorrhage, possibly due to a ruptured corpus luteum cyst. Temperature 99° F., pulse 88, blood pressure 100/72, white blood cell count 12,000, hemoglobin 90 per cent. Immediate operation was performed.

Operation (Feb. 12, 1937): supravaginal hysterectomy, bilateral salpingo-oophorectomy, release of adhesions. Operative diagnosis: tubal pregnancy, left, with tubal rupture; myomas of the uterus; follicular cysts of ovary, bilateral; pelvic and omental adhesions. Drains: none.

At operation about 200 c.c. of free blood was found in the peritoneal cavity. Some of it was very fresh. The uterus contained many small myomas, the largest being about 3 cm. in diameter. There were many adhesions between the omentum, the pelvic organs, and the pelvic floor. Both Fallopian tubes were open. There was a small brownish mass situated just proximal to the fimbriated extremity of the left tube, and fresh arterial blood was spurting from a fine vessel at a small ruptured point in this mass. The diagnosis of ruptured tubal pregnancy was thus obvious. Both ovaries contained follicular cysts and were about 3 cm. in diameter. The whole pelvis and all the pelvic viscera were injected. There was a diffuse injection of the pelvic peritoneum which was attributed to the irritating effect of the blood. Tuberculous salpingitis was not suspected in the operating room. Because of the pathologic condition of all the pelvic structures supracervical hysterectomy and bilateral salpingo-oophorectomy were done. No difficulties were experienced during this procedure.

The hospital convalescence was uneventful. As soon as the pathologic slides were seen the diagnosis of tuberculous salpingitis and endometritis was made. We then had the lungs examined by x-ray, and the findings were normal.

Pathologic study (Gyn. Path. No. 44501) showed (Fig. 1) the uterus to be of normal size, shape, and consistency except for a pedunculated firm nodule 2 cm. in diameter on the posterior surface and a few smaller generally distributed subserous nodules. The serosa was roughened by a few hemorrhagic adhesions. The uterine cavity was normal except that the endometrium, which averaged 2 mm. in thickness, had a slightly roughened and hemorrhagic surface. The right tube contained a small accessory ostium near the fimbriated end and was of average length and diameter except for a nodular appearance at several points; its serosa was slightly injected. On section the wall was thickened and the lumen was small but patent and filled with bloody friable substance (Fig. 1, *A*). The right ovary was about normal in size, shape, and appearance. On section it contained a few small cysts, some old scars, and a large corpus luteum of pregnancy (Fig. 1). The left tube

was of about normal dimensions except that it was nodular at points (Fig. 1, *B*). Distally it contained a globular enlargement which on section consisted of a mass of solid hemorrhagic granular substance with a small gestation sac in the center (Fig. 1, *C*). The sac wall was thin and white, the sac contained some slightly blood-tinged watery fluid and its lining was smooth and shiny. No fetus could be found. The left ovary was large and contained a follicular cyst and several small atretic follicles.

Microscopic study showed that the endometrium was thin and its stroma was fibrous. The epithelial elements were normally present. The glands were present in the usual number, were of average uniform diameter, and the epithelial cells lining them showed no secretory activity. No decidual reaction was seen. At one point the stroma contained a few definite tubercles around which there was a rather dense infiltration of lymphocytes and an occasional giant cell with coronal nuclei

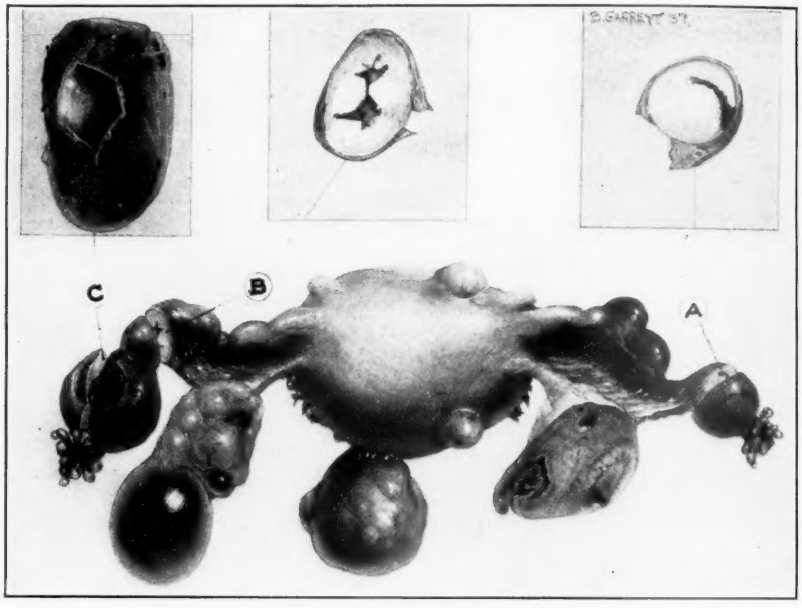

Fig. 1.—(Gyn. Path. No. 44501.) The entire gross specimen, as removed at operation, viewed from above. Note the tortuosity, injection, and nodular thickenings of both tubes, with the "potato sack" appearance of the distal ends of the tubes. The sections *A* and *B*, through the tubes, show the extensive scarring and thickening of the walls as the result of the tuberculous infection. Although distorted, the lumina remain open. Section *C* is through the pregnancy in the left tube, and shows the gestation sac surrounded by old organized blood clot and the scarred and partially necrotic tube wall.

(Fig. 2). The myometrium was normal except for a few small myomas. The serosa was slightly hypervascular and thickened. The lumen in the proximal third of the left tube was rather small and was surrounded by a thick layer of tissue made up of small cystic glands imbedded in a scarred and dense fibrous stroma (Fig. 3). The lumen and glands were lined with a single layer of columnar tubal epithelium, except for a few places where it was piled up into 2 or 3 layers. The scarred stroma between the matted mucosal folds contained many tubercles and Langhans' giant cells (Figs. 3 and 4). The muscularis was thin and intact. The serosa was thickened, scarred, hypervascular, and contained a few nests and germinal centers of lymphocytes. A section through the nodular structure in the distal portion of the left tube showed the wall to be thinned out and the serosa was scarred and infiltrated with lymphocytes. The mucosa was absent, being replaced by some scarred

and partly necrotic solid tissue infiltrated with lymphocytes (Fig. 5). A few partly necrotic chorionic villi were imbedded in the wall and normal trophoblastic epithelium covered about half of their surface. There was some slight semblance of decidual reaction around a few of the villi at the more viable points. The muscularis was sparse and infiltrated with lymphocytes. The left ovary contained Graaffian follicles, atretic follicles, and corpora albicantia. The right tube showed tuberculosis (Fig. 6) similar to that in the left tube. The right ovary contained a corpus luteum of pregnancy.

Fig. 2.

Fig. 3.

Fig. 2.—(Gyn. Path. No. 44501.) High power detail of a tubercle in the endometrium. Note also the complete absence of secretory activity and hyperplasia in the epithelium of the endometrial glands just above the tubercle. (×200.)

Fig. 3.—(Gyn. Path. No. 44501.) Section through part of the left tube at a point about 1 cm. proximal to the site of the pregnancy. The matting together of the mucosal folds with resultant cystlike spaces lined with tubal epithelium, the scarring and thickening of the mucosal stroma, and the tubercles show that the process is extensive and typical tuberculous salpingitis. (×80.)

Fig. 4.—(Gyn. Path. No. 44501.) High power detail of a tubercle in the mucosa of the left tube. Note, as in Fig. 2, the centrally located Langhans' giant cell (*A*). (×200.)

The final diagnosis was: ruptured tubal pregnancy left, tuberculous salpingitis bilateral, tuberculous endometritis, myomas of the uterus, accessory tubal ostium right, follicular cysts ovary left, peri-oophoritis chronic, corpus luteum of pregnancy ovary right, and pelvic and omental adhesions.

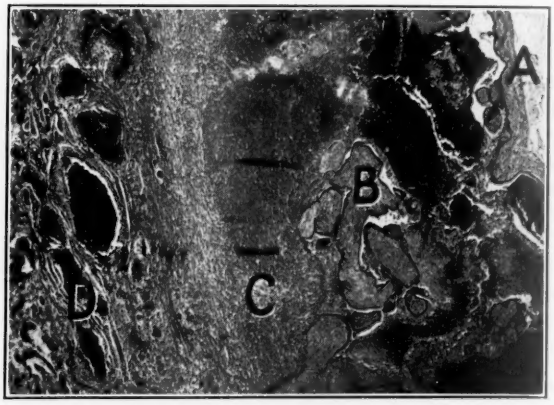

Fig. 5.—(Gyn. Path. No. 44501.) Section through the ruptured pregnancy near the distal end of the left tube. In the upper right corner can be seen part of the cavity of the gestation sac and its wall (*A*). Some partly necrotic chorionic villi (*B*) are seen lying imbedded in the densely scarred and chronically inflamed granulation tissue which had replaced the mucosa and most of the wall of the tuberculous tube (*C*). The avascularity of this scarred area would indicate that the trophoblast was poorly nourished. On the left is seen the scarred, thickened, and vascular serosa (*D*) (×30.)

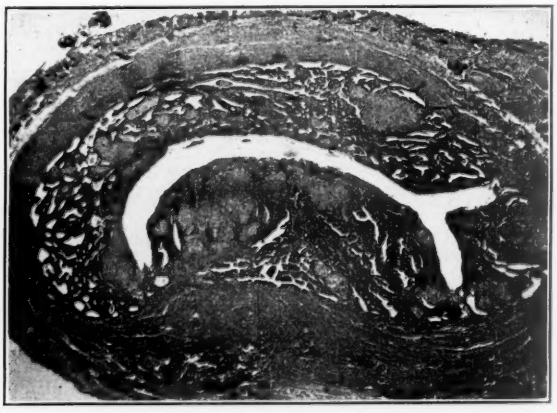

Fig. 6.—(Gyn. Path. No. 44501.) Low magnification cross section of the left tube taken about 1 cm. distal to the cornual end. Despite the extensive tuberculous process the lumen of the tube is open. At some points the lumen is lined only with chronic inflammatory granulation tissue with an ulcerated surface, and it is readily seen that a fertilized ovum passing down the tube would certainly not be in an environment favorable and nutritive to its life and development. A section from a similar portion of the right tube shows an identical picture. (×20.)

Fourteen months after operation this patient was in better health than she had ever experienced. For the past year she has had none of the old lassitude and fatigue, and no longer feels the need of afternoon rest. Although there were no signs of tuberculosis elsewhere, the patient was given careful instructions about rest, sunshine, and diet. There were practically no menopausal symptoms.

* * * * *

There are a very few cases where tuberculosis and pregnancy have been found in the same tube and in which the diagnoses have been confirmed by pathologic study of the operative specimens. In going through the literature we have found the following cases: Acconi,[5] Alexander and Moszkowicz,[6] Bovin (2 cases),[7] Ferroni,[8] Freericks,[9] Kröner,[10] and Höppner.[11] Höppner gives a very complete pathologic description of his case and a good general discussion of the subject. His patient was a 35-year-old housewife who had not menstruated for six weeks when first seen. She complained of severe acute lower abdominal pain and was in shock. A laparotomy was immediately done and the abdomen was full of blood. The left Fallopian tube contained a nodular structure about 2 cm. in diameter at the ampullar end and there was fresh bleeding from the ostium. The tube was resected and the patient made an uncomplicated recovery. Pathologic study showed some thickening of the tube at the ampullar end, and the lumen was patent. Microscopic study showed many tubercles in the masses of adherent and scarred mucosal folds, and there was a small blood-filled sac in the ampullar nodule with chorionic villi growing into the adjacent muscularis. The actual developing embryo, at about the six-week stage, was found attached to the anterior wall of the sac. There was pronounced proliferation of the trophoblastic epithelium.

In the cases of Freericks, Bovin, Höppner, and ourselves, the pregnancy was within the lumen of the tube and nidation had taken place in the general vicinity of active tuberculous infection of the mucosa. In the cases of Acconi, Alexander and Moszkowicz, and Kröner, the pregnancy was found at the ostium or cradled by the fimbriae alone. Schröder and Rau,[12] Shober,[13] Mossa,[14] and Therkelsen[15] have described cases where there was bilateral tuberculous salpingitis, and an ectopic pregnancy mass was adherent between an ovary and the adjacent tube. In the case of Schröder and Rau, the pregnancy was 6 cm. in diameter and was adherent to the mesosalpinx of the left tube and to the surface of the adjacent ovary. Despite marked fairly fresh tuberculous salpingitis, the lumina of both tubes were patent. Curiously enough the right ovary contained a corpus luteum of pregnancy and the left ovary was small and contained no cysts. This indicates (as in the authors' case) external migration of the ovum, but here it definitely was fertilized while en route. Microscopic study showed decidual changes in the endometrium and in the fimbriae of the left tube. The chorionic villi were found only in the serosa of the left mesosalpinx and tube and over part of the surface of the left ovary. Werhatzky reported a case[16] with tuberculous salpingitis in which there was an advanced abdominal pregnancy. Taylor[17] mentioned that he had found tuberculous salpingitis in 42 out of 86 cases of tubal pregnancy, but there were no pathologic studies to support this opinion. Such an occurrence is certainly contrary to the experience of all who have studied either tuberculous salpingitis or tubal pregnancy.

According to the literature, the simultaneous occurrence of tuberculosis and pregnancy in a Fallopian tube is a rarity indeed. In our laboratory only 1 in every 115 cases has been tuberculous salpingitis, while 1 in every 90 cases has been tubal pregnancy. When these two conditions themselves occur with such infrequency, the laws of chance would make their concurrence extremely rare. We have seen it but once in 46,700 cases. The chief significance of the finding of these two conditions simultaneously is the bearing out of the theory that mechanical obstruction to the descent of the fertilized ovum in the tube is the chief cause of tubal pregnancy.

SUMMARY

1. A case of simultaneous tubal pregnancy and bilateral tuberculous salpingitis is presented. It is the ninth in the world literature, and is one in which there was external migration of the ovum. The clinical and pathologic aspects of the case are treated in detail.

2. The great rarity of these cases is thought to be due to: (a) The obstruction of the lumen of the tube to any passage of spermatozoa and ova (if ovulation is taking place). (b) The lack of nutrition from the diseased tubal mucosa to the

transient fertilized ovum (with resultant death of the ovum) if the lumen is open. (c) The lack of tubal mucosa healthy enough to allow successful nidation of the fertilized ovum if it is trapped in the tube.

3. The literature dealing with the subject is reviewed.

* * * * *

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PRIMARY MALIGNANT MELANOMA OF THE VULVA

W. O. Johnson, M.D., F.A.C.S., Louisville, Ky.

(From the Departments of Gynecology and Pathology, University of Louisville Medical School)

PRIMARY malignant melanomas of the vulva are very rare growths. This growth may occur at any age, but most frequently occurs between the ages of forty and fifty years, usually appears as a firm, nontender nodule in the labia, enlarges rapidly, metastasizes, and ulcerates early, leaving a discharging, necrotic, ulcerated surface. It may arise from connective tissue, subcutaneous tissue, muscle of round ligament, fibroma, or other structures.

The diagnosis is made before ulceration occurs by biopsy. After ulceration it must be differentiated from ulcerated fibroma, granuloma inguinale, lymphogranuloma inguinale, and carcinoma. Malignant melanoma metastasizes by blood and lymph channels and any or all organs may be involved early. The prognosis is more unfavorable than in carcinoma of the vulva. Patients rarely live over six months, averaging less than a year. Seven per cent cures are reported in the early cases. The therapy is similar to that of carcinoma of the vulva.

The following case is presented because of the rarity of such a growth:

S. B., white, widow, 42 years of age. First admitted to Gynecological Dispensary, Louisville City Hospital, Nov. 27, 1935, complaining of a growth on the right side of vulva, nervousness, weakness. She had been married twelve years, husband died of typhoid fever. Three children, living and well; one miscarriage (five months) last pregnancy. Nine years ago, she had excision of ovarian cyst; general health otherwise good.

Menstrual history normal until one year ago; since then, every three months, and painful. Last period Nov. 20, 1935. In the past year has been taking antisyphilitic therapy, no history of other venereal disease.

Present Illness.—Sept. 25, 1935, noticed a marblelike lesion on right side of external genitalia. This has never been red or sore. After a week's growth, it broke and discharged thin, watery fluid. Since then the growth has increased rapidly in size. In the past week, has had a very odorous discharge, and has had enlargement and dull, heavy pains in right groin; nocturia and some dysuria. In past week, patient has grown quite nervous, weak, and has been unable to sleep because of pain and odor.

Physical Examination.—Nov. 27, 1935: Well-developed and well-nourished woman of 42 years. Temperature: 99.4° F.; pulse, 86; respirations, 27.

The abdomen showed a midline scar; no masses or tenderness. The right inguinal glands were the size of olives, tender, fixed and no evidence of fluctuation. Left inguinal glands enlarged, but not tender.

Large, necrosing, cauliflower-like growth, size of pint milk bottle, arising from the right labial region, involving the upper three-fourths of right labia major and minor; was fixed, and tender to touch, quite friable with three or four areas of necrosis over the surface the size of a dime; bled freely to touch; some areas were covered with a thick, necrotic membrane. Urethra was not involved, left labia apparently normal. The vagina showed congestion; cervix was essentially normal; uterus anterior and fixed; no other abnormalities made out in the pelvis.

Red blood cells, 3,730,000; white, 12,000; hemoglobin, 75 per cent; Wassermann, negative. Urine analysis: Specific gravity, 1.009, amber, acid in reaction; albumin one-plus; many red blood cells and pus (probably from vaginal discharge).

Nov. 30, 1935: Biopsy report: diagnosis, melanosarcoma, Grade IV.

Dec. 5, 1935: Right vulvectomy with resection of right inguinal lymph glands.

Operative Note.—Triangular area of the skin was removed from the right groin going wide of the involved inguinal and femoral nodes. Dissection was carried over across the center portion of the mass, down including the clitoris and right half of the mass, and circling around the urethra and including the right half of the vulva, down to within one inch of the rectum. Lateral line of incision was in the folds of the thighs. Bleeding points were coagulated and dissection of the femoral and inguinal lymph nodes was started, including the fascia of the external abdominal wall and over the region of the vulva. Dissection around the superficial saphenous vein revealed it to be involved in the growth. The wall was stripped back as far as it could be felt, but it was not deemed advisable to manipulate the vein with the possibility of dislodging the material. The involved lymph nodes were removed together with the vulva in one mass. Bleeding points were coagulated with the coagulating current after resection of the area. Skin edges were loosely approximated with kaldermal stay sutures. Retention catheter was placed in the urethra, and the patient returned to the ward in good condition.

Pathological Report.—Through the courtesy of Dr. A. J. Miller, Dr. H. Gordon, and Dr. H. H. Sweets, of the Department of Pathology, the following pathologic reports were made:

Biopsy specimen was a mass of tissue measuring 2.5 by 2 by 2.5 cm. There was no capsule. It was soft and somewhat friable. The color was gray except for brown areas due to old hemorrhage.

Sections consisted entirely of neoplastic growth (Fig. 1). The cells had round to oval nuclei which had sharp outlines and chromatin arranged in delicate strands and fine granules. In some areas the nuclei were elongated and stippled. A few have large nucleoli. A moderate number were in mitosis. The cytoplasm stained densely with eosin. A few cells were polygonal, but most of them were stellate or elongated, resembling somewhat the shape of smooth muscle cells; others had long, coarse processes. Occasional cells were huge and some of these were multinucleated. There were a few small scattered areas of pigment deposit, some of which was evidently derived from hemoglobin, but some was questionable. Special stains for iron revealed small, fine, granular masses of brown pigment in some of the cells. It was, therefore, considered as melanin.

The cells were arranged in interlacing bundles. There was no palisading. The stroma was very small in amount except for a few large trabeculae. There were numerous small blood vessels which consisted of an endothelial lining supported by a very small amount of connective tissue. The parenchymal cells were sometimes arranged radially about the strands of stroma.

The specimen was an elliptical piece of skin including part of the vulva and to which was attached an ulcerating tumor mass, subcutaneous fat, fascia, and several lymph nodes. The tumor measured 11 by 6 by 4 cm. and had ulcerated the skin. It was light gray in color except for localized yellow areas due to necrosis and

brownish portions where hemorrhage had occurred. The lymph nodes were large, firm, and light colored as if invaded by tumor growth.

The microscopy was identical with that of the previous specimen except that there were a few more mitotic figures, the structure was a little more cellular, and there was less fibrillar substance. There was infiltration at the periphery of the growth, but the border was quite definite and there was some pressure atrophy about it. The pigment was small in amount, but was demonstrable (Figs. 2 and 3).

The ulceration of the skin had resulted from invasion by the tumor. There was no suggestion that the squamous epithelium or that of the skin glands was the source of the tumor. The lymph nodes were partly destroyed by metastatic growth.

Dec. 6, 1935: 100 r. daily x-ray treatment for twenty days: Posterior pelvis, 1,400 r.; anterior pelvis, 1,400 r.; total, 2,800 r.

The patient made a most satisfactory convalescence; the wound healed well; the patient was discharged from the hospital on Jan. 2, 1936, in good condition. She was entirely free from pain in the groin, gained in weight and was up and about her work in usual health until May 7, 1936, when she noticed a lump appear just

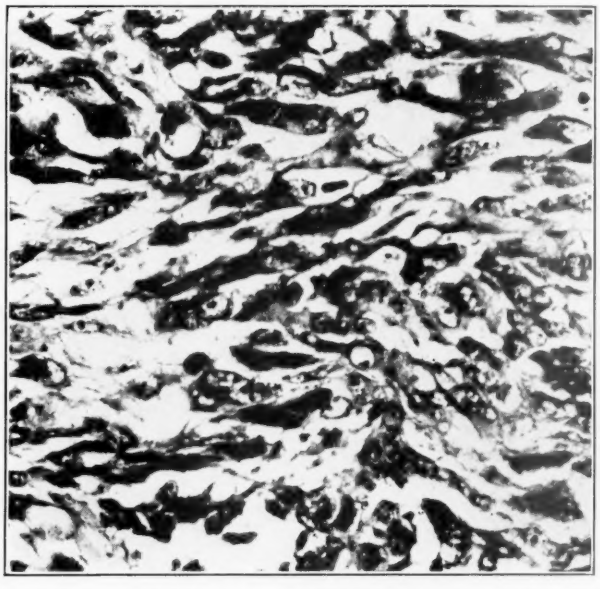

Fig. 1.—High-power photomicrograph of primary tumor. The cells have eosin-staining cytoplasm which is elongated and continuous with that of adjacent cells. A very few small granules of melanin were found.

under the eleventh rib, right axillary line. Examination showed subcutaneous mass 6 cm. in diameter at the right eleventh costal margin, with enlargement of mass in right inguinal region. There were some small shotlike glands in the right axilla.

May 18, 1936: X-ray films showed that the patient had extensive metastatic masses throughout both lung fields, and eleventh and twelfth ribs, right, with rapidly growing recurrence in right groin and areas over the chest wall.

June 14, 1936: Patient died at 1:35 A.M. following convulsive seizure with generalized metastasis.

Autopsy.—The body was in a fair state of nutrition. In the region of the right mid-axillary line at the level of the tenth rib was a tumor mass measuring 8 by 3 cm. It was not attached to the rib or the skin and was slightly soft. A number of masses were palpable in the right lower quadrant and there were enlarged firm lymph glands in each groin. The wound was well healed and no tumor was found in the scar.

There was some displacement of the liver downward, the lower border being 8 cm. below the ribs in the midclavicular line. Each diaphragmatic dome was lowered slightly. Beneath the periosteum of the bodies of the seventh and eighth thoracic vertebrae and also beneath the periosteum of the right second, third, fourth, and seventh ribs, there were tumor masses 1 to 3 cm. in diameter, firmly embedded in the tissue and invading the bone.

The heart weighed 250 gm. There were a few petechiae in the pericardium. The mitral leaflets contained two small sclerotic plaques, but they caused no demonstrable interference with function.

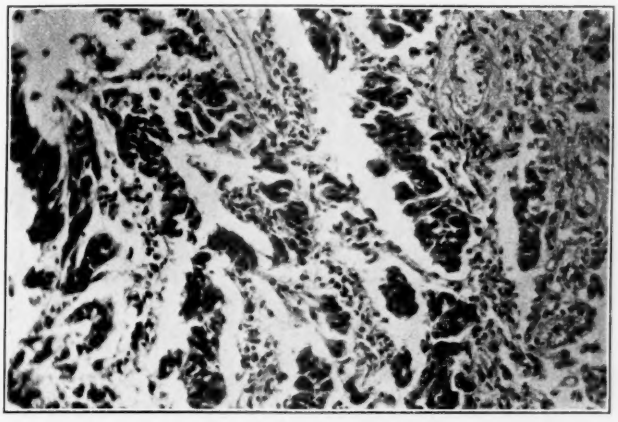

Fig. 2.—Low-power photomicrograph of lung metastasis. Several alveoli contain masses of tumor cells which are grouped to resemble epithelium.

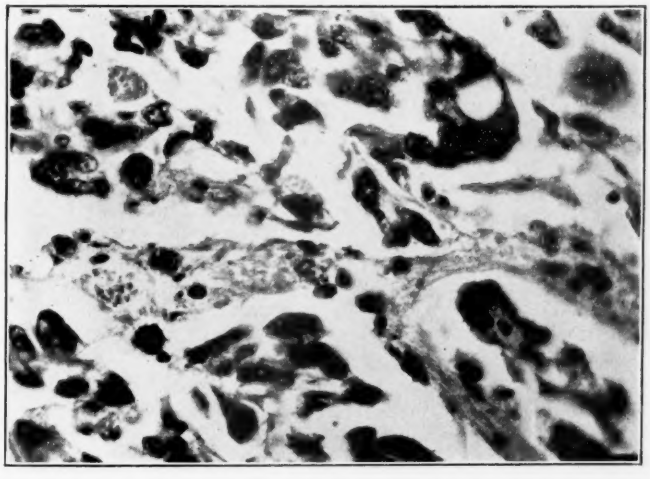

Fig. 3.—High-power photomicrograph of brain metastasis. The cells here have less cytoplasm, and are less uniform. Granules of melanin can be seen in the cytoplasm of several cells.

The nuclei of the muscle cells were pyknotic and there was moderate cloudy swelling.

The right lung weighed 380 gm., the left 400. There was slight edema in the posterior portions. Throughout the substance of each lung there were numerous tumor nodules, 1 cm. or so in diameter. They were yellow gray in color, soft, the sectioned surfaces were blotched with old hemorrhage. The central portions were

necrotic. The central part of the left lower lobe was soft, greenish in color, and smelled putrid. Partial obstruction of the bronchus, by a large neoplastic lymph node at the hilus, had evidently contributed to the gangrene. Most of the hilus nodes were enlarged by tumor growth so that they measured from 1 to 3 cm. in longest diameter.

Sections of the lung revealed microscopic abscesses evidently contributed to by pressure from the tumor nodules. The tumor nodules were rich in parenchyma cells which, at the periphery of the growths, were growing in the lumina of the air sacs with no new stroma at all. The cells were elongated, had a moderate amount of eosin-staining cytoplasm with a very few stubby processes. They were in compact masses with imperfect palisading. Occasionally there were layers of columnar cells arranged like epithelium. Mitotic figures were in moderate numbers. Small masses of brown pigment (melanin) were frequently seen in the cytoplasm. There were a few tumor giant cells. In the center of the nodules the lung was destroyed and a small amount of new stroma had developed.

The liver weighed 1,950 gm. The organ was strewn with tumor nodules varying from those barely visible to others 1.5 cm. in diameter. They were under some pressure. The liver substance was light colored, soft and was moderately mottled from chronic passive congestion.

Sections revealed neoplastic structure identical with that in the lung except there was more stroma, giant cells were more numerous, and melanin was abundant. There was some pressure atrophy about the growths. There was slight damage from passive congestion.

The spleen weighed 400 gm. The substance was soft. Throughout the tissue 15 tumor masses 1 to 4 cm. in diameter were found, 4 of these were present in the capsule.

The structure of these nodules was identical with those elsewhere.

The kidneys weighed 180 gm. each. In the cortical substance of each organ there were several tumor masses, each of which was a few millimeters in diameter. In the upper pole of the right one a tumor 1 cm. in diameter was found.

Sections showed the tumor to be the same structure with a small amount of melanin. The tubule cells were moderately damaged by cloudy swelling.

The left adrenal was normal in size, but its sectioned surface showed it to be partly replaced by a tumor tissue. The right one was enlarged by a tumor mass 5 cm. in diameter which evidently began in the medulla and expanded the adrenal so that the gland tissue formed a capsule.

This tumor was identical with the others. Melanin was abundant.

The lymph nodes of the abdomen were enlarged moderately, especially those in the region of the pancreas and the sentinel node of the gall bladder.

Sections showed these to be badly damaged, some to be completely replaced by tumor growth. Here the tumor cells were arranged about the blood vessels. Pigment was present.

The gastrointestinal tract and pancreas contained no tumor tissue. The appendix had been removed surgically.

The uterus was small. In the wall of the body was a hard, spherical, encapsulated tumor mass 5 mm. in diameter, evidently different from the other tumors found.

Sections of this tumor showed it to be made up of interwoven bundles of smooth muscle fibers identical with those of the uterine muscle. There were also numerous glands lined by tall columnar epithelium and supported by stroma similar to that of the endometrium. The structure was that of an adenomyoma.

The right uterine tube and ovary were absent evidently from surgical procedure. The left tube and ovary, the bladder, and pancreas appeared normal.

The thyroid gland showed no changes grossly, but sections revealed several tumor thrombi in large veins and capillaries. The cells were the same type as those in other tumor nodules, but were pyknotic. There was no stroma. It appeared that the masses in the veins were extensions from those in capillaries, though the gland was not invaded.

In the skull at the vertex there was an irregular opening about 8 mm. in diameter. Just beneath this was a tumor mass 2 cm. in diameter. The defect was the result of tumor growth beginning beneath the dura and invading the bone. In the left parietal region was a second extradural tumor 1.5 cm. in diameter, but the inner table of the skull was only roughened.

The convolutions of the brain were moderately flattened from pressure. In the leptomeninges were numerous dark spots resembling old hemorrhage. Coronal sections revealed numerous tumor masses in the cortex, white matter, in the pons and cerebellum. These varied in size from those barely visible to 8 mm. in the pons and 2 cm. in the cerebellum. The tumor was soft, gray, friable tissue into which some hemorrhage had occurred.

Sections revealed the same structure here as elsewhere, except the cells resembled epithelium more, and melanotic pigment was very abundant. There was no new stroma. A number of blood vessels had extensions of tumor growth about them in the perivascular lymph spaces. There was much hemorrhage in and about some of the growths.

SUMMARY

The primary illness consists of a malignant melanoma arising in the skin of the right labia majus, extending into the subcutaneous tissues, to the skin of the pubic region and vulva, and metastasizing to the regional lymph nodes, lymph nodes of the abdomen and chest, liver, spleen, adrenals, kidneys, lungs, brain, and skeleton.

The derivation is, by reasoning and not by demonstration, from the chromatophores of the skin. The immediate cause of death is pulmonary infection consisting of small multiple abscesses near metastatic tumor growths and gangrene of the left lower lobe contributed to by partial obstruction of the bronchus by a large neoplastic lymph node at the hilus.

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908 BROWN BUILDING

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Marcel is of the opinion that gonorrheal vulvovaginitis in young girls is more than a vulvovaginitis because it involves the ureters, the cervix and sometimes also the rectum. The disease is not rare. It has a definite social importance because it may interfere with the future genital life of the child.

Local therapy requires a long time, it is difficult and has many failures. Estrin therapy has not yet become popular in France in spite of its successes, especially in the acute cases.

J. P. GREENHILL

PRIMARY LYMPHANGIOMA OF THE FALLOPIAN TUBE

S. Sanes, M.D., and Robert Warner, A.B., Buffalo, N. Y.

(From the Pathological Laboratories of the Buffalo General Hospital and the University of Buffalo Medical School)

PRIMARY lymphangioma of the Fallopian tube is a rare neoplasm. Complete review of the literature discloses 17 cases reported to date.[1-14] Of these, only 3 are found in American Journals.[5, 8] Moreover, of practical importance is the histologic interpretation of certain tumors, classified as lymphangioma, in regard to potential malignancy. We, therefore, wish to present the pathologic findings in an additional case of primary lymphangioma of the Fallopian tube.

Clinical History.—M. T., a white, married woman, 55 years of age, was admitted to the Buffalo General Hospital July 8, 1937 in the service of Dr. Ralph Upson complaining of "a tumor in the abdomen" for one and one-half years. With appearance of the tumor, the patient experienced a heavy sensation in the lower abdomen. There had never been definite pain. Frequency of urination and nocturia were present. In the past year the patient had lost 12 pounds in weight.

Except for a normal delivery in 1911, the obstetric history included no other pregnancies.

Menstruation began when the patient was fourteen years of age. Periods were regular, every twenty-eight days and four or five days in duration. After the abdominal tumor was noticed, periods became irregular. There was menorrhagia and metrorrhagia. The last menstrual period occurred June 25, 1937. The mother of the patient died of a growth in the abdomen.

Physical Examination.—Temperature, pulse, and respiratory rates were normal. The patient was a well-developed, white woman, apparently in good health. Lungs were clear and resonant. Heart rate was regular; no murmurs were heard. Abdomen showed no scars. In the lower half, there was distinct bulging. Here palpation revealed a large mass, which was irregular, hard, and movable.

Laboratory Work.—Urinalysis, serologic and blood chemistry examinations disclosed no relevant findings.

The clinical impression was fibroid uterus.

Operative Report (Dr. Ralph Upson, July 9, 1937).—Low midline incision. A large, grapefruit-sized fibroid uterus was found. One fibroid on the posterior surface, which extended deeply into the pelvis, was adherent to the rectum and had to be dissected therefrom. The left tube and ovary were also bound by adhesions. Hysterectomy with left salpingo-oophorectomy was made. The right tube and ovary were apparently normal.

Postoperative Course.—Following operation, the patient developed purulent drainage from the abdominal wound, which gradually subsided. Patient was discharged from hospital Aug. 2, 1937.

Gross Description of Surgical Specimens.—Corpus uteri with attached left tube and ovary was received. The corpus was myomatous. It weighed 850 gm. and measured 19 by 13 by 8 cm. The gross structure was distorted by multiple fibroids. The 3 largest were intramural and measured 4, 6, and 7 cm. in diameter. In the fundus was a walnut-sized fibroid. Several smaller submucous and intramural fibroids were scattered throughout. The endometrium was not hyperplastic; it measured 0.2 cm. in thickness.

The ovary measured 4 by 3 by 1 cm. It contained a corpus luteum with central hemorrhage and a corpus hemorrhagicum.

The Fallopian tube was 11 cm. long. The fimbriated end was patent. At a point 8 cm. from uterine attachment, there was observed in the upper wall an apparently

circumscribed nodule 1.1 cm. in diameter. The overlying peritoneum was stretched, smooth, and glistening. The nodule was solid and cut with moderate consistency. On section the nodule bulged outward. The color was whitish. The cut surface had a peculiar "papillary" or pitted character. The lumen of the tube at the site of the nodule was markedly compressed. In the remainder, the wall of the tube was not thickened; the lumen contained no exudate.

Histologic Description of Surgical Specimens.—Microscopic examination of uterus and ovary confirmed the gross findings. Fibroids were typical leiomyomas.

The nodule in the left Fallopian tube was fixed in 10 per cent formaldehyde and imbedded in paraffin. Sections were cut at 5 and 7 micra. Hematoxylin-eosin, Van Gieson, Mallory anilin blue-acid fuchsin, Weigert elastic, mucicarmine, and thionine blue staining and modified Bielschowsky silver impregnation methods were carried out.

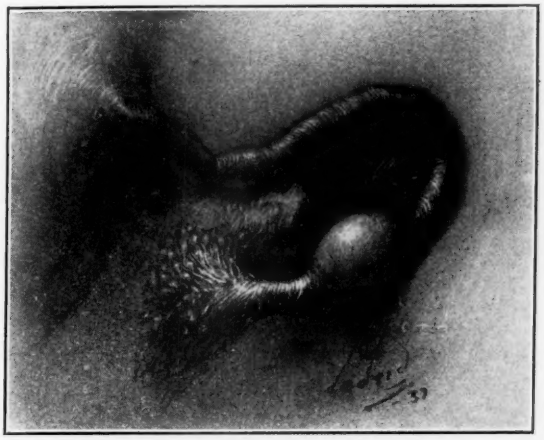

Fig. 1.—Gross appearance of lymphangioma of Fallopian tube.

On microscopic examination, the nodule, noted grossly, was situated in the wall of the tube between tunica propria, muscularis and subserosa. The muscle layer was practically completely replaced; only at the outer parts of the nodule could a few muscle fibers and bundles be seen. Though, with low power, the nodule appeared somewhat circumscribed, it was not encapsulated. Its borders merged actively into surrounding tissue of tube.

In general, the histologic picture of the nodule itself was that of a meshwork of channels or spaces ranging from capillary to cavernous in size with moderate stroma. The large spaces were distributed chiefly in the central portion. The representative lining of spaces consisted of single flat endothelial cells. For the most part the nuclei were slightly plump, oval with their chromatin material arranged in fine dots. Some nuclei were thin and hyperchromatic. There were no prominent nucleoli. In certain spaces the lining in addition to typical endothelial elements possessed cuboidal and polyhedral cells. Their cytoplasm stained lightly and was fairly abundant. Nuclei were moderately large and oval. Cell outlines were not distinct. Free margins were not sharp but feathery; cytoplasmic festoons of syncytial nature projected into lumens. True cilia were not seen. In many spaces the lining was composed entirely of tall (cuboid-cylindrical-polyhedral) cells such as just described. Not infrequently these cells appeared stratified. They also exhibited budding proliferation into lumen. Few lumens were nearly filled with desquamated and proliferating cells. The rather frequent presence of endothelial giant cells in the lining was also noted. Lining cells also showed atypical nuclei.

The lumens were for most part free. Or they contained a thin slightly acidophile fluid and cells with round or indented nuclei. Rare eosinophile cell was seen. In many lumens cells corresponding to desquamated endothelial cells were observed.

Mucus stains (controlled by sections from normal appendix, under same fixation) were completely negative for mucus both in cells and in lumens.

The stroma in certain areas was edematous. In other parts it was dense and cellular. The cells were not fibrocytes, but were elements concerned with the tumor itself. The appearance of the stroma imitated the structure seen in angioblastic and reticulo-endothelial neoplasms. The cytoplasmic outlines of the cells referred to could not be distinctly made out. The cells were moderately large and oval and polyhedral in shape. They could be recognized by large, oval faintly staining nuclei. Syncytial processes with reticular connections between cells were evident. Cells were also arranged in solid masses and cords. Canalization was sometimes taking place.

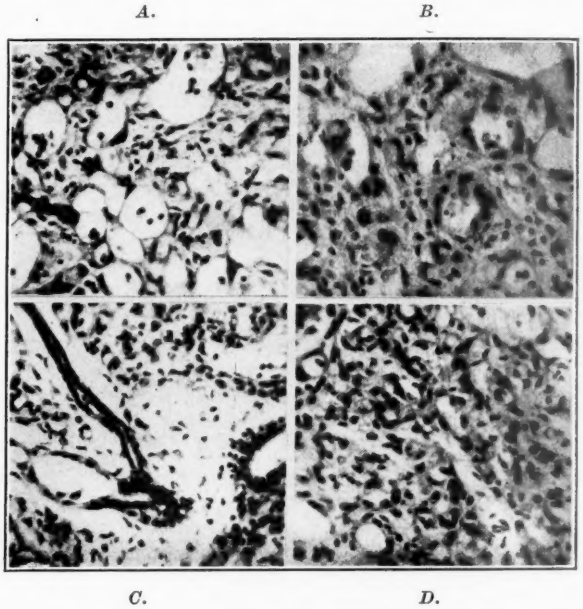

Fig. 2.—*A*, Spaces lined by endothelial cells with round cells and desquamated endothelial cells in lumens. Endothelial giant cells are shown. (High power.) *B*, Spaces show tall and large cells with huge dark, and multiple nuclei. (High power.) *C*, Tumor growing into mucosa, showing lymphatic space contrasted with 2 glands. (High power.) *D*, More cellular part of stroma with capillary formation. (High power.)

Cytoplasm of cells in stroma exhibited rare vacuolation. The number of collagen fibers in the stroma was small. Most of the fibers were reticular and elastic in nature. The reticulum fibers did not surround spaces as a definite basement membrane but encircled them, and continued as reticulum fibers of the stroma, running between cells. Scattered in stroma were round cells, eosinophiles and neutrophiles. In one area of the nodule there was focal infiltration, in addition, of plasma cells and hemosiderosis. The stroma possessed small arteries and thin-walled blood capillaries of its own.

The mucosa overlying the tumor was stretched. Epithelial cells were columnar, cuboidal, and flat. Villi were preserved only in a few places. Tunica propria of these showed a few round cells; beneath the stretched mucosa there was infiltration of round cells, and neutrophiles, edema and recent hemorrhages. Few glands extended into tunica propria. The distinction between tumor spaces and glands was not difficult.

In outer part of tumor were focal collections of round cells in a network of reticulum. The growth, as previously described, invaded both mucosa, subserosa, and adjacent muscle fibers. No calcification was observed.

The histologic diagnosis was lymphangioma with distinct endothelial proliferation. Because of this proliferation, together with replacement of muscle fibers and invasion into mucosa and subserosa, it was felt that the tumor had to be considered malignant from an histologic aspect.

COMMENT

We feel that the lesion of the Fallopian tube which we describe is justifiably diagnosed as lymphangioma for various reasons. Grossly, it forms a definite, more or less circumscribed nodule within the wall of the tube. Microscopically the fundamental structure is one of small and medium-sized spaces which are lined by flat endothelial cells, and which contain no erythrocytes, but for the most part mononuclear cells, and thin fluid. Endothelial giant cells are seen. The stroma possesses a cellular architecture seen in angioblastic tumors. Its fibrillar element is composed chiefly of reticular and elastic tissue. Collagen fibers are sparsely distributed. The reticulum which surrounds spaces does not form a strictly defined basement membrane, but blends continuously with reticulum in stroma. Interstitial round cell infiltration is present; finally, follicular collections of round cells with reticular network appear in peripheral zone of the nodule.

Of practical interest, from the standpoint of histologic diagnosis, is the presence of cells in the lining of a good number of spaces which are much taller than flat endothelial cells. Though at first glance such a feature might lead one to search for an epithelial character in the neoplasm, we believe that this microscopic finding may be honestly reconciled with the diagnosis of lymphangioma. For, on close examination, "tall" cells are discovered only in a portion of spaces, or along with flat cells in the lining of a single space. The minute structure of these cells and their relation to exfoliated cells in lumens, to the stroma, and to glands of mucosa do not support an epithelial origin. With controlled staining methods mucus could not be demonstrated within lining cells or in lumens. In addition, histologists accept the view that endothelial cells harbor the biologic propensity to assume varying gradations of tall forms. Such conversion manifests itself in inflammatory and neoplastic processes in endothelium of lymph and blood channels. Cuboidal and cylindrical cells have been described in previous cases of lymphangioma of the Fallopian tube, notably, those of Höhne,[1] Dienst,[2] Kermauner,[3] Franz,[4] Dietrich,[7] Schiffman,[12] Nicod,[13] and Szathmáry.[14]

Of further practical interest, not only from the point of view of histologic diagnosis but also from the basis of prognosis, are certain microscopic evidences of endothelial proliferation, besides change in height of lining cells, e.g., stratification and desquamation of lining cells, atypical nuclei, giant cells, and blastoma-like stroma with solid nests and cords, apparently undergoing canalization.

Although any of these may be seen some time in simple, mature lymphangiomas, they must be interpreted, when found to an appreciable extent, as speaking for an embryonal, actively proliferating tendency. As a matter of fact, Kermauner wondered whether the degree of endothelial proliferation, which he considered was especially marked in his case, and in the two instances reported before him did not warrant placing so-called lymphangioma of the Fallopian tube in the category of endothelioma. Since Kermauner's paper, however, out of 10 cases[5-7, 12] with adequate histologic descriptions have shown rare or no signs of endothelial proliferation. Indeed, review of the literature reveals that lymphangioma of the Fallopian tube can be classified into two histologic groups: (1) lymphangioma with rare or no endothelial proliferation (2) lymphangioma with slight to distinct endothelial proliferation (lymphangio-endothelioma?).

That the discussion of the foregoing paragraph involves something more than a hair-splitting distinction is borne out by two statements. In every case of lymphangioma of the Fallopian tube reported in the literature, which showed rare or no endothelial proliferation (despite destruction of tubal tissue and lack of encapsulation), the neoplasm was considered innocent. In certain cases,[1-4, 11] on the other hand, with acknowledged endothelial proliferation this finding along with that of

replacement or destruction of normal tissue of the tube and with that of mergence or invasion into surrounding issue was taken as histologic ground for expression of an opinion of "malignancy." Now what meaning shall be placed on such histologic evaluation in regard to the practical problem of clinical prognosis? In answer to this question, we must note that the cases definitely appraised as histologically malignant possessed certain features grossly which bespoke a localized lesion. The tumor was small. It was discovered only as an incidental finding in women operated upon for other causes. The peritoneum overlying the tumor was not perforated. Metastases were not found. Whether patients, subsequent to extirpation of these small lymphangiomas, followed the course of a benign tumor, as suggested by the gross findings, or of a malignant blastoma, as adjudicated by microscopic examination, cannot be determined because of the total lack of follow-up reports in the literature. In Aschheim's third case where besides showing destruction of muscularis and mucosa, the lymphangioma approximated a child's head in size, gave symptoms and physical signs, and evoked a gross impression of malignant tumor, the patient was entirely well one year after excision. Kermauner's suspicion, however, that perhaps some cases labeled "carcinoma of the Fallopian tube" might actually be endotheliomas has to be mentioned. In view of the facts, then, that only a few cases of lymphangioma of the Fallopian tube with acknowledged endothelial proliferation have been recorded, and that information relative to postoperative course in these cases is lacking, the problem of correlating histologic findings with clinical prognosis must be left open. One can yet speculate, as apparently Schiffman[12] and Szathmáry[14] did, whether the tumor under discussion may not be of a type which calls forth an histologic opinion of malignancy but which, at least, in the stage thus far seen, and with regard to metastases, acts biologically in a benign manner.

On the other hand, Nicod[13] precludes the necessity of a consideration, such as outlined in the preceding paragraph, by classifying recorded cases of so-called lymphangioma of the Fallopian tube so that neoplasms with endothelial proliferation are separated from simple lymphangiomas and designated "reticulomes" or "reticuloendotheliomas." For Nicod,[13] these tumors comprise a distinct pathologic entity. Originating in mesenchyme with angio- and lymphoblastic potentialities, they occur in the Fallopian tube and in the male genital organs, and run a silent, benign course.

In the seventeen recorded cases of primary lymphangioma of the Fallopian tube, the race was apparently always white. Where information was given, the ages ranged from 30 to 86 years. Six patients were more than 50 years old.[4, 8, 10, 12, 13, 14] The tumor occurred in nulliparas[4, 9, 14] as well as in multiparas.[3, 7, 11] In 14 cases, it was discovered incidentally at operation for pelvic lesions which produced symptoms, e.g., leiomyoma of uterus,[1, 2, 3, 5, 9, 11, 14] carcinoma of ovary[12] and uterus,[4] fibroma of ovary[8, 9] and retroflexed uterus;[7, 8] in 2 cases,[10, 13] at autopsy, in patients who died from cardiac decompensation. On one occasion[9] the lymphangioma reached a size large enough to call for surgical therapy. The isthmic, middle and ampullary parts of either tube were fairly equally involved. The pathologic findings in our case can serve to illustrate the average gross and histologic description from the literature. In 2 cases[3, 13] calcification was noted microscopically.

Theories concerning the etiology and pathogenesis of primary lymphangioma of the Fallopian tube are purposely omitted from our paper. In regard to them reference can be made to the reports of Silva[10] and Nicod.[13]

SUMMARY

The literature on primary lymphangioma of the Fallopian tube, which includes 17 cases, is reviewed. The pathologic findings in an additional specimen, found accidentally in the left salpinx of a 55-year-old white, married woman operated upon for a fibroid uterus, are described. Attention is drawn to the histologic classifications of lymphangioma of the Fallopian tube on the basis of descriptions of the recorded cases. The importance of correlating these classifications with pathologic and clinical

data in future cases from the points of view of histogenesis and biologic behavior of the neoplasms under discussion is implied.

We are indebted to Dr. Ralph Upson for permission to transcribe the clinical record.

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PRIMARY CARCINOMA OF THE FALLOPIAN TUBE

D. Nelson Henderson, M.B., Toronto, Ont.

(From the Department of Obstetrics and Gynecology, University of Toronto)

THE first authentic case of primary carcinoma of the Fallopian tube was described in 1888 by Orthmann.[1] It is a rare disease, only 3 cases occurring in 30,000 gynecologic admissions in the Bellevue Hospital in New York.[2] Charache[3] in 1936 reviewed the literature from 1888 to 1935 and discovered only 323 cases. It is therefore of more than usual interest that we encountered on the Public Ward Service of the Toronto General Hospital 2 cases within a period of fourteen months.

Case 1.—*Primary bilateral carcinoma of Fallopian tubes.* The patient, Mrs. T., 57 years of age, was admitted to the Toronto General Hospital in September, 1933. Her chief complaints were irregular slight vaginal bleeding of four months' duration. The menopause had occurred seven years previously. She had had one full-term pregnancy thirty-two years ago, followed by pain in lower abdomen which gradually disappeared in the ensuing years. There were no further pregnancies. The patient's mother died from carcinoma of the breast.

Physical examination revealed a healthy-appearing white female looking much younger than her stated age. Abdominal examination was negative except for slight lower abdominal tenderness on deep palpation. Pelvic examination revealed atrophic external genitalia. The cervix was slightly eroded and a small polypus protruded from the external os. The body of the uterus was slightly irregular in shape. A cystic mass the size of an orange was palpated in the right fornix. No mass was felt in the left fornix.

A preoperative diagnosis of cervical polypus and ovarian cyst was made and a provisional diagnosis of carcinoma of the endometrium. At operation the cervical polypus was removed, the cervix dilated, and the uterine cavity curetted. Small thin fragments of endometrium were obtained. The cervix was cauterized. The abdomen was opened and the uterus found to contain small myomas. Both tubes were closed, retort-shaped and adherent to the ovaries. The right ovary was replaced by a cyst the size of an orange. Bilateral salpingo-oophorectomy and supravaginal hysterectomy were performed. The patient made an uneventful recovery and left the hospital apparently well in seventeen days.

Pathologic Report.—Specimen: Uterus, tubes, ovaries, polypus.

Gross Description: A small uterus 4 cm. in length with atrophic wall in which three small myomas were present, the largest measuring 1.5 cm. in diameter. One

was calcified. The left tube was thin-walled with lumen dilated to a diameter of 1.5 cm. and was filled with a grayish colored, papillary friable growth attached to tubal wall throughout its whole extent except in the isthmic portion. The fimbriated end of the tube was closed. The right tubal lumen was dilated to a diameter of 3 cm. and was filled with a similar growth. The right tube was adherent to the ovary and the fimbriated end was closed. The ovary was replaced by a cyst 6 cm. in diameter, filled with clear fluid, and lined by a smooth glistening lining. Left ovary was atrophied.

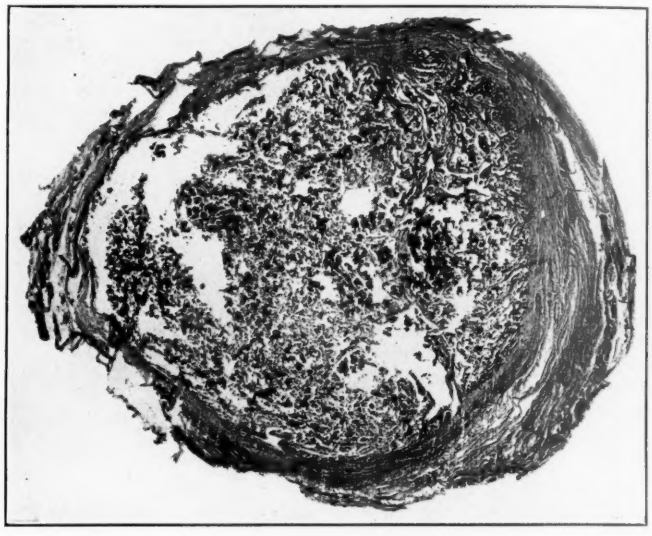

Fig. 1.—Case 1. Very low power of cross section of tube, showing general lacelike pattern of the carcinoma.

Fig. 2.—Case 1. Microphotograph medium power, showing piling up of malignant cells supported on a scant delicate stroma.

Microscopic Report.—The uterine muscle bundles and endometrium were atrophic. The myomas presented the usual microscopic picture. The polypus had a fibrous tissue stroma studded with multiple gland spaces lined by typical endocervical epithelium.

Both tubes showed lumen dilated by a papillary overgrowth of tubal mucosa, the papillas of which in many areas had fused together, giving a lacelike pattern to the growth (Fig. 1). Cells in some areas closely resembled tubal epithelium while in others they were round and oval and were growing in solid masses and in a pseudogland-like manner (Figs. 2 and 3). Invasion of the thin wall of the tube,

Fig. 3.—Case 1. High power microphotograph of Fig. 2, showing variation in size of cells, complete loss of polarity and mitotic figures.

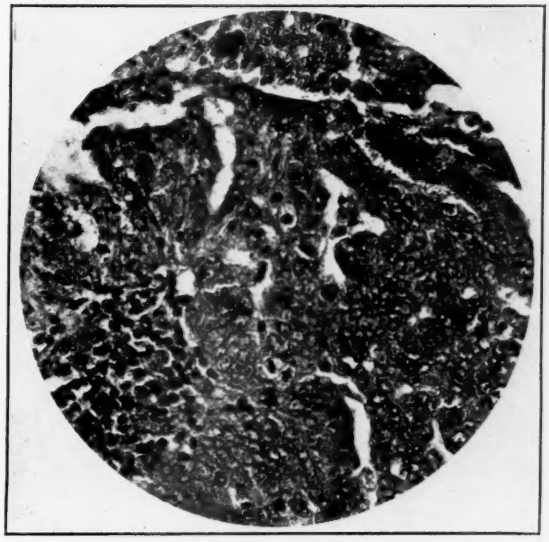

Fig. 4.—Case 1. High power microphotograph of secondary carcinoma of cervix.

by slender cords of malignant cells, had occurred. Throughout the central portion of the tumor multiple small areas of calcification were present. Mitotic figures were numerous and supporting stroma was very scant.

The cyst of the right ovary was lined by a single row of low cuboidal cells. The left ovary was atrophic.

Diagnosis.—Primary bilateral carcinoma of Fallopian tubes, myomas of uterus, cervical polypus, simple serous cyst of ovary (right).

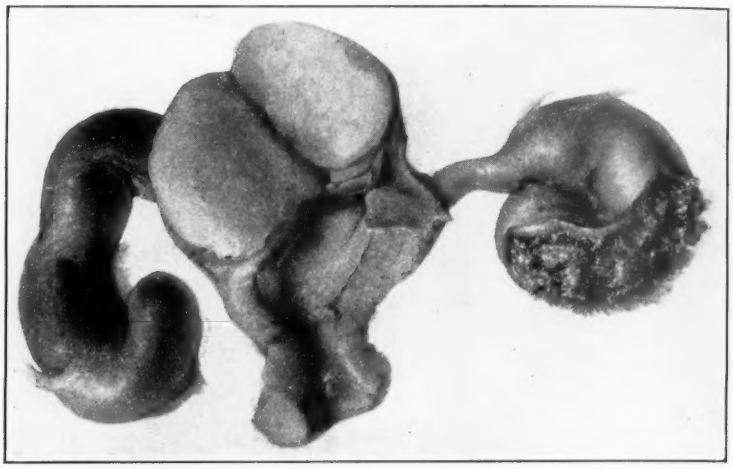

Fig. 5.—Drawing of gross specimen, Case 2, primary carcinoma of left tube.

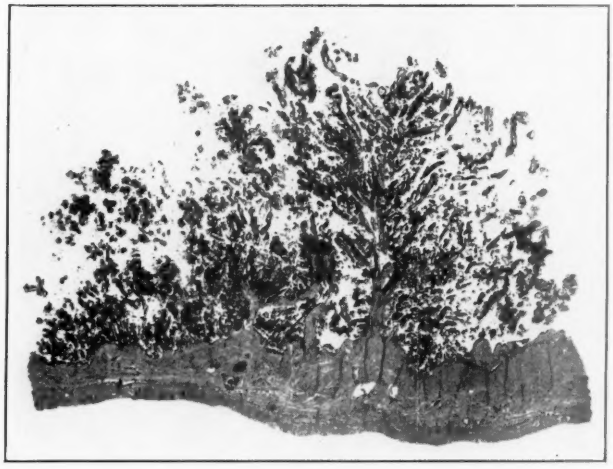

Fig. 6.—Case 2. Very low power microphotograph, showing treelike pattern of tumor growth.

Patient did not return for observation as instructed until July, 1935, at which time she complained of loss of strength, and slight vaginal bleeding of seven months' duration. Examination revealed a large firm cervix, freely movable with a normal appearing vaginal aspect. The patient was examined under anesthesia. The pelvis was free from evident tumor masses, but on dilatation of the cervical os, the cervix was found almost completely replaced by tumor growth (Fig. 4) which had left an intact vaginal surface covered by normal appearing mucosa. Radium was inserted into the cervical canal and a dose of 4,000 mg. hours was given, followed

by a series of high voltage x-ray exposures to the pelvis. The patient remained well until March, 1937, when she began to lose weight and strength. In May she developed a persistent dry cough and x-rays of chest showed widespread secondary tumor. The patient died Sept. 7, 1937, four years after her original operation.

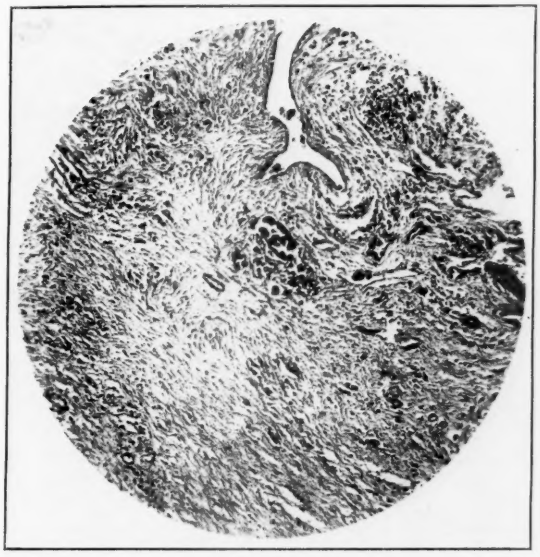

Fig. 7.—Case 2. Low power microphotograph, showing invasion of tubal wall close to serosa by malignant cells.

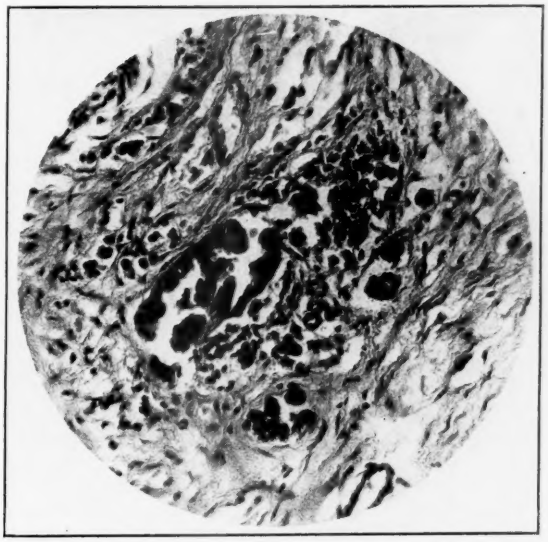

Fig. 8.—Case 2. High power microphotograph of invasion of wall of tube as shown in Fig. 7. Some cells appear to be in lymphatic spaces.

CASE 2.—Patient, aged 57 years, was admitted to the Toronto General Hospital in November, 1934. Her chief complaints were slight continuous vaginal bleeding and discharge for five weeks, general weakness for three months. Menopause had occurred ten years previously. Patient was married at 37 years of age and had never been pregnant.

Examination revealed a healthy-appearing female not acutely ill. Abdominal examination was negative. Pelvic examination revealed a nulliparous vaginal outlet and healthy small cervix. There was slight blood-stained discharge coming from cervical os. Uterus was enlarged, irregular, and freely movable. In the right fornix a soft tumor mass the size of a tangerine orange was palpable. It was not tender.

A preoperative diagnosis of ovarian neoplasm was made. Patient was examined under anesthesia and curettage revealed no evidence of carcinoma of the endometrium. The abdomen was opened and both tubes were found to be enlarged, closed, and retort-shaped. Numerous adhesions were present. Uterus contained a myoma in the fundus. Bilateral salpingo-oophorectomy and total hysterectomy were performed. Patient made an uneventful recovery from the operation and left the hospital fourteen days later.

Pathologic Report.—Specimen: Uterus, tubes, ovaries, and cervix (Fig. 5). Uterus and cervix measured 10 cm. in length. The fundus was occupied by a firm fibroid 4 cm. in diameter, and the cervix was small and atrophic. The endometrium was thin and partially curetted. The right tube was converted into a small retort-shaped hydrosalpinx 2.5 cm. in diameter. A few delicate adhesions were present. The left tube was narrow in isthmic portion but dilated in ampulla to a diameter of 3.5 cm. by a fine papillary growth. The lumen contained a small amount of blood-stained fluid.

Microscopic Report.—Uterus: Muscle bundles were atrophic and endometrium was senile.

Left Tube: Sections revealed the lumen filled with a fine papillary treelike growth of tubal mucosa (Fig. 6). The papillas were slender and covered by columnar and cuboidal epithelial cells. Variation in size, shape, and staining qualities was marked. The nuclei were hyperchromatic and mitotic figures were infrequent. Cells were irregular in arrangement, piled up several layers thick and in some areas seemed to be growing without evident supporting stroma. The tubal wall was deeply invaded by clumps of malignant cells (Figs. 7 and 8) some of which appeared to be lying in the lymphatic spaces. The right tubal wall was thin and atrophic, the plicae had disappeared and the epithelium was flattened.

The patient remained well until October, 1937, approximately three years after her operation. Beginning in October she noticed a gradual increase in the size of her abdomen. Examination revealed the abdomen markedly distended by free fluid (250 ounces at the last paracentesis) in which clumps of malignant cells were evident on section. Multiple small hard tumor nodules were palpable in the abdomen after paracentesis. X-ray of the chest showed no evidence of secondary carcinoma. The patient died in March, 1938.

DISCUSSION

These two cases of primary carcinoma of the Fallopian tubes are reported as rare and interesting gynecologic malignancies.

The clinical histories, progress of the disease, and gross specimens are similar in all major respects to the cases previously reported. In both specimens microscopic examination revealed fairly deep invasion of tubal wall and in one, malignant cells in lymphatic spaces. As in both cases the fimbriated ends of the tube were sealed off, it would appear that initial spread of the malignancy was by lymphatics or direct extension through the wall of the tube.

It seems highly probable from a review of the literature and a study of these two cases that previous tubal inflammatory disease is of some etiologic significance. The gross appearance of the tubes in these cases strongly suggests previous salpingitis. Both patients gave a history of a long period of sterility. The first case had symptoms of a mild post-partum pelvic inflammation after the birth of her only child. The second case had definite salpingitis in the tube, not the site of the malignancy.

The poor prognosis of carcinoma of the Fallopian tube is confirmed by the progress of these two cases. The probability of preoperative diagnosis is slight as there are no symptoms characteristic of malignancy in this site. The symptom, vaginal bleeding, is one common to carcinoma in most situations in female genital tract.

The operative treatment employed in the first case, supravaginal hysterectomy and bilateral salpingo-oophorectomy was obviously incomplete as within a year and a half, secondary carcinoma developed in the cervix. Despite the inadequacy of the operative treatment employed, this patient lived longer than the second patient. At the present time it would seem that bilateral salpingo-oophorectomy and total hysterectomy followed by high voltage x-ray therapy is the form of treatment that offers the best prognosis in this disease.

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170 St. George Street

PUERPERAL HEMORRHAGE IN CHIMPANZEES*

James H. Elder, Ph.D., Orange Park, Fla.

(From the Yale Laboratories of Primate Biology)

In a recent descriptive account of pregnancy and parturition in a chimpanzee[1] brief mention was made of a slight hemorrhage occurring fifteen days after delivery. Subsequent observations of other individuals, the records of previous cases, and a few references to this phenomenon in the literature, indicate that it may be a typical characteristic of the early puerperium in chimpanzees. The observations may be of interest to gynecologists because they are unique. I have been unable to find any clinical reports of a similar nature.† The phenomenon also has not been reported for any other primates.

In his description of the first birth of a chimpanzee in captivity, Montané[3] (1915) states that sixteen days after birth there was a normal return of catamenia with an abundant flow for twenty-four hours. This bleeding may have been normal for a chimpanzee, but it certainly did not represent the return of catamenia. Following this no bleeding was observed for months. Undoubtedly it was of the same origin as the bleeding described in the present report. In a case (the birth of Cuba) observed by Senora Rosalía Abreu, but hitherto unreported, bleeding occurred twelve days after parturition. One other instance of puerperal bleeding of the type described herein is noted by Fox[2] in his account of a chimpanzee birth at the Philadelphia Zoological Gardens. The comment is brief: "Eleven days after delivery of our chimpanzee there was a bloody fluid seen once, about midday."

Post-partum hemorrhage within twenty-four hours is commonly observed and is easily accounted for. Our interest here is in bleeding which occurs, certainly as a direct consequence of, but several days following parturition. As a rule the total amount of the vaginal flow is not large and usually does not continue for more than forty-eight hours. Quantity

*The writer gratefully acknowledges the aid of the Committee for Research in Problems of Sex, National Research Council.

†Apparently it is not homologous to the true hemorrhage associated with endometritis post partum as described by Frankl. (*Frankl, Oskar:* Arch. f. Gynäk. **129:** 87, 1926.)

and duration correspond, in most cases, to not more than a third of an average menstrual flow. In some cases it may be seen macroscopically for only a few hours and is easily overlooked unless frequent, careful search is made. The discharge is usually dark red, sometimes quite thin, and occasionally contains small blood clots.

Table I is a summary of the observations of puerperal hemorrhage made in these laboratories. For the purpose of comparison, the three cases observed elsewhere are also included. The table shows 16 out of 18 cases in which the phenomenon appeared on the ninth to sixteenth day after delivery.

The appearance of this bleeding has never been associated with any manifestation of pain or discomfort. It seems to be unrelated to age, parity, the general health or physiologic status of the individual. In short, the temporal relation to parturition is the only noteworthy characteristic, although it should be added that the length of gestational interval may be a determining condition. The bleeding was not observed in any of 13 early and late abortions.

TABLE I. PUERPERAL HEMORRHAGE IN CHIMPANZEES

CASE	NAME AND NO. OF ANIMAL	DATE OF PARTURITION	TIME OF BLEEDING (IN DAYS, POST-PARTUM)	REMARKS
1	Josie (30)	July 15, 1933	9, 10, 11, and 17	
2	Wendy (4)	Jan. 16, 1936	9	Premature (202 days*)
3	Nana (6)	May 2, 1934	10	
4	Mimi (44)	Oct. 15, 1936	10, 11 and 12	Premature stillbirth (167 days*)
5	Pati (42)	Mar. 27, 1937	10, 11, 12, and 13	
6	Pati (42)	May 14, 1933	11	
7	Soda (12)	May 5, 1937	11, 12, and 14	
8	Wendy (4)	Jan. 18, 1938	12	
9	Mona (36)	June 26, 1933	12	A twin birth
10	Mona (36)	June 26, 1936	15	
11	Josie (30)	Oct. 7, 1935	15, 16, and 21	An old blood clot or bit of placental tissue seen
12	Dita (40)	Apr. 13, 1937	15 and 16	
13	Nana (6)	Jan. 19, 1938	15 and 16	
14	May (32)	Nov. 10, 1937	18	Infant removed day after birth; no lactation
15	Cuba (46)	Apr. 11, 1935	20	Did not accept infant; no lactation
	Cucusa	Apr. 27, 1915	16 and 17	Observed in the Abreu primate colony, Havana, Cuba
	Mona	Mar. 24, 1926	12	Observed in the Abreu primate colony, Havana, Cuba
	Marianne	Oct. 1, 1928	11	Observed in the Philadelphia Zoological Garden
			Median time of appearance 12	

*Conception age.

It would be easier to account for this type of hemorrhage if histologic descriptions were available and if more were known of the process of involution of the uterus in chimpanzees. It seems probable that the bleed-

ing may coincide with an advanced stage of involution. In man the uterus undergoes a reduction of about two-thirds in size by the end of the second week of the puerperium. As the corpus resumes its normal size and again becomes a pelvic organ, expulsion of small quantities of blood and bits of retained placental or decidual tissue might be expected. Cases 14 and 15 add something to the validity of this explanation. It is well known that lactation facilitates the process of involution. The delay in appearance of the phenomenon in these two cases is associated with absence of lactation. In each case the infant was taken from its mother the day after birth.

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CONGENITAL TRANSVERSE SEPTUM OF THE VAGINA COMPLICATING PREGNANCY*

ARTHUR M. DAVIDS, M.D., NEW YORK, N. Y.

(From the Department of Obstetrics, Morrisania City Hospital)

A CONGENITAL transverse septum of the vagina is one of the rarer anomalies which may complicate pregnancy and cause dystocia. A review of the literature reveals a comparatively small number of cases. Brickner[1] in 1903, quoted Neugebauer[2] as having collected 56 cases from the literature in which cesarean section was performed, and 237 cases in which delivery was completed by various means through the vaginal route. Two hundred and seven of these cases were due to acquired atresia or stenosis of the vagina.

The remaining 86 cases could be attributed to congenital anomalies of the vagina and only a very small number of these cases had an anatomic description which resembled that of "transverse vaginal septum." Since 1895 there have been 37 true cases of congenital transverse septum described, 23 complicating pregnancy and 14 in the nongravid patient. I shall describe two additional cases of the congenital type. In both instances a careful history was taken to eliminate any such causative factors as inflammation or trauma of mechanical or chemical nature.

CASE 1.—(No. 87583.) M. M., a 27-year-old white female, was admitted to the Morrisania City Hospital on Feb. 22, 1937, because of vaginal bleeding. The patient gave the following history:

She could not recall having had any illness except measles and chicken pox, and the only previous surgical history was that of a tonsillectomy in 1934. The onset of her menstrual periods occurred at the age of twelve years, each period lasting four days and recurring regularly at intervals of twenty-eight days. During the first two days of her period, she had marked dysmenorrhea. There was no history of a previous vaginal discharge or vaginal trauma. She was married in April, 1936, and on questioning, it was found that she had experienced dyspareunia from the onset of her marital state to the present time. Her menstrual periods had been regular until July 16, 1936, and then she developed amenorrhea. After six to eight weeks she had mild morning nausea and occasional vomiting, and took for granted that she was pregnant. At about this time she noticed that there was a very slight amount of vaginal spotting which occurred almost daily, but never suf-

*Read at a meeting of the Section on Obstetrics and Gynecology, New York Academy of Medicine, May 25, 1937.

ficient to cause the patient alarm. This continued until February 21, when following coitus, she began to bleed vaginally, and passed a few small clots. She came to the hospital the following morning and was still bleeding very slightly.

The patient was a well-nourished white female who did not look acutely or chronically ill. Her color was good and she exhibited no signs of excessive blood loss. General physical examination was negative, except for the obstetric condition.

The uterus was enlarged to the size of a six and one-half months' gestation. There was no area of tenderness nor could any contractions be felt. A fetus with the vertex presenting was felt abdominally, and the fetal heart heard in the left lower quadrant.

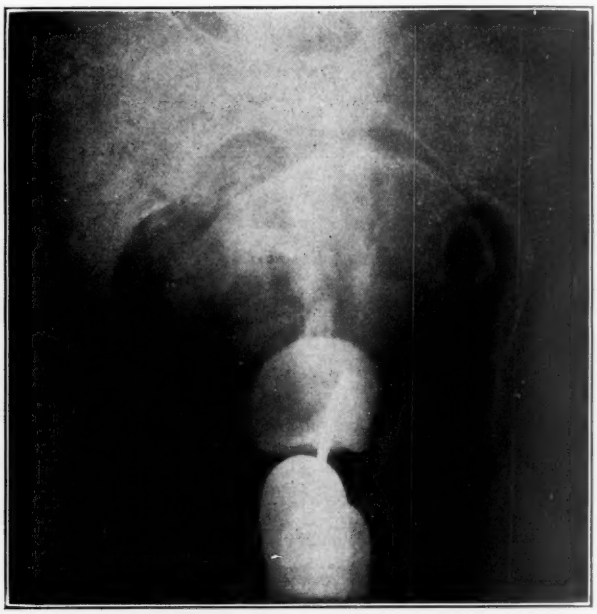

Fig. 1.—Anteroposterior view with lipiodal filling the cavity above the transverse septum.

A vaginal examination was deferred until the patient was typed and a blood donor available, in view of a possible placenta previa. The vaginal examination revealed normal external genitalia with remnants of a torn hymen. The introitus admitted two fingers and after passing into the vagina about 6 cm. the examining fingers impinged upon a smooth vault behind which a conical cervix could be felt. There was no narrowing of the vagina from its entrance to the vault.

A speculum was inserted and a transverse vaginal septum situated at about the junction of the middle and upper thirds of the vagina was visualized. There was a central orifice about ½ cm. in diameter. The margins of the orifice were eroded and bleeding. Pelvic measurements were normal. After a short period of hospitalization the vaginal bleeding ceased. The space behind the septum was distended with lipiodol, and an x-ray showed a space equal to about one-third the length of the vagina. The patient was referred to the prenatal clinic, and was again admitted to the hospital shortly before term. She went into labor on the evening of April 25. The vertex was fully engaged in the left occipitoposterior position. The patient had weak and irregular pains and the cervix was only 2½ fingers dilated at the end of twenty-four hours when her pains ceased completely. She had no pains during the following twenty-four hours, and the cervical dilatation remained stationary. Uterine contractions were renewed during the evening of April 27, and on the following morning

at 6 A.M., the cervix was fully dilated with the vertex impinging upon the septum. The orifice of the septum was now dilated sufficiently to admit a finger, and it was found that the septum was about ½ cm. in thickness at the edge of the orifice and increased to a thickness of 1½ cm. at its lateral attachments. The septum was incised at the areas of 8, 10, 2, and 4 o'clock, and Elliot forceps applied to the head which had rotated spontaneously to an anterior position and was low in the midpelvis. A living male infant weighing 8 pounds 12 ounces was delivered. The placenta and membranes were delivered intact by the Credé maneuver, and the vagina was then packed tightly with iodoform gauze to control bleeding. The total blood loss was approximately 350 c.c. The patient's condition was excellent and she required no further treatment. The packing was removed after twenty-four hours and there was no vaginal bleeding. The patient had an afebrile puerperium and vaginal examination on the tenth day revealed a vagina of normal depth and width without any constriction in the area of the pre-existing septum. The uterus was well involuted and the cervix had a small bilateral laceration. There was no evidence of any laceration of the vaginal walls and the only remains of the septum were a few small tabs, about ½ to 1 cm. in length. The patient was discharged in good condition.

CASE 2.—O. S., a 33-year-old negress, was referred from the prenatal clinic for study on March 3, 1937. On her first visit to the clinic it was discovered that she presented a vaginal anomaly. The patient gave the following history:

She had suffered from no illnesses except measles and occasional upper respiratory infections. The patient had the onset of her menstrual periods at the age of eleven years, having a three-day flow and an interval of twenty-eight days. Her periods were always regular and she experienced moderately severe dysmenorrhea during her entire period. There was no history of any inflammatory disease or vaginal discharge. The patient has been married fourteen years and has never used contraceptives, since she wanted to have a child. She always experienced slight dyspareunia. The patient had a regular menstrual period in October, 1936, and since then has had amenorrhea.

The patient was a well-developed healthy negress, and the general examination was negative, except for the obstetric and vaginal condition. The uterus was enlarged to the size of a five months' gestation and a small ballotable fetus was present. The external genitalia were normal and the remnants of a torn hymen were present. The introitus admitted two fingers easily which passed to a depth of 6 to 7 cm. when they impinged upon a smooth vaginal vault behind which a conical cervix could be felt. The vagina was broad and not constricted below this vault. A speculum was inserted and revealed a smooth membranous vault which appeared to have a median raphe with a small pin point opening in each half of the septum. A small probe could be passed through the left orifice but not through the right one. However, during x-ray studies with lipiodol, the fluid was seen to escape through the latter orifice. Because of this, the space could not be distended as well as in the previous case. X-rays, however, did show a good collection of lipiodol behind the septum.

The patient was again admitted to the hospital on July 10, 1937, with the history of the onset of labor at 8 P.M. July 9, with the membranes intact. Physical examination revealed a uterus of term size with a vertex presentation in the left occipitoposterior position and the head low in the midpelvis. The cervix was one finger dilated (rectal examination). After forty-three hours of active labor the cervix was fully dilated and the vertex low in the midpelvis still in the posterior position. Under general anesthesia, the septum was seized with two ring forceps and it split open radially in all directions, having become very thin during the progress of labor. A Scanzoni maneuver was employed to deliver a living infant, weighing 6 pounds 10 ounces. The total blood loss was approximately 350 c.c., and after the placenta and membranes were delivered intact, the vagina was packed with iodoform gauze. The packing was removed after twenty-four hours and there was no further bleeding. The patient had an afebrile puerperium and on discharge on

the tenth day the uterus was well involuted and only a few small tabs of mucous membrane could be found high up on the vaginal wall at the site of the former septum. There was no vaginal constriction.

The author wishes to express his appreciation to Dr. Harry Aranow, Director of the Division of Obstetrics and Gynecology, for his technical advice and assistance.

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EXTRA- AND INTRAUTERINE PREGNANCY

FRANK J. CLARKE, A.B., M.D., BROOKLYN, N. Y.

THE coexistence of intrauterine and extrauterine pregnancy is sufficiently rare to justify the report of two additional cases.

CASE 1.—B. R., a 27-year-old married woman, was admitted to the Brooklyn Hospital Nov. 22, 1934, complaining of pain in the right lower quadrant of the abdomen of six days' duration and slight vaginal bleeding of three weeks' duration. The patient had missed one period four to five months previously (she did not remember which). The following three to four periods were normal as to time, duration, and amount of flow. The period due three weeks before admission began on time, but the flow continued with slightly more profuse bleeding the day of admission. Six days previously the patient first noticed a dull aching pain in the right lower abdominal quadrant. There was no radiation of the pain, but on sudden coughing or sneezing, the pain became sharp and stabbing. There had been no nausea or vomiting, no urinary symptoms and no leucorrhea. At the time the pain began the patient developed a coryza, followed by a cough.

The past personal history was negative except for a pregnancy eight years previously, which resulted in identical twins.

The admission temperature was 99.2° F., pulse 80, respirations 18, and blood pressure 118/65.

The positive physical findings were: (1) A few râles at the base of the right lung posteriorly. (2) Tenderness on deep palpation over McBurney's point, but no muscular spasm or mass. (3) On vaginal examination, a boggy uterus, enlarged to the size of an eight weeks' gestation, a hard but gaping cervix, not tender on motion, and some sensitivity but no mass, high in the right fornix. There was dark blood on the examining finger.

The blood count showed hemoglobin 67 per cent, red blood cells 3,250,000, white blood cells 11,400 with 87 per cent of polynuclears. The sedimentation time was over two hours. Urinalysis was negative.

The patient was given medication for her upper respiratory infection. The right lower quadrant pain disappeared, but the patient continued to spot. The white blood count at this time dropped to 10,000 with 80 per cent of polynuclears, and the sedimentation time was over three hours.

The patient was examined under avertin, gas, and oxygen anesthesia with findings the same as at the previous examination, except that a small, firm, movable mass was felt in the right adnexal region. The cervix dilated easily and the cavity of the uterus measured six inches. Portions of what appeared grossly to be placental tissue were removed from just inside the internal os, with an ovum forceps. Because of the size of the uterine cavity (which was larger than would be expected with an ectopic pregnancy), plus what appeared to be placental tissue, the patient was considered to have had an incomplete abortion, and a laparotomy was not done. The postoperative course was normal, but the patient continued to spot a very small amount of dark blood. She was discharged from the hospital six days postoperatively.

Pathologic report showed shaggy fragments of early placenta. Chorionic villi were present. Sections showed evidence of placenta.

The patient was seen at home four days after her discharge from the hospital because of vague lower abdominal discomfort and continued slight spotting. The blood pressure and pulse were normal, but she had had an evening rise of temperature to 99.2° F. Abdominal examination was negative. The pain subsided with rest in bed, but the evening elevation of temperature continued, associated with increasing constipation.

On the eleventh day at home the lower abdominal pain increased and the patient was unable to void. Her bowels had not moved in the preceding forty-eight hours. A vaginal examination, after catheterization, disclosed a tender, fluctuant mass, the size of an orange, in the culdesac.

The patient was readmitted to the hospital December 16. The temperature was 100.6° F., pulse 94, respirations 26, blood pressure 112/60. Blood count showed 3,000,000 red blood cells with 66 per cent hemoglobin and 16,640 white blood cells with 94 per cent polynuclears. The sedimentation time was twenty minutes.

A posterior colpotomy was performed and between three and four ounces of dark red blood were obtained. A culture of this blood was reported sterile.

The patient continued to spot and four days later she was discharging a small amount of bright red blood. A laparotomy performed the following day, disclosed a right-sided ruptured ectopic pregnancy. The broad ligament was edematous and the site of a considerable number of adhesions. A right salpingo-oophorectomy was done. A transfusion of 500 c.c. of whole blood was given postoperatively.

The convalescence was satisfactory and the patient was allowed home on the fifteenth day postoperative. At this time her hemoglobin was 75 per cent with 3,860,000 red blood cells.

Pathologic examination showed an ovoid mass 3.5 by 4.5 cm. in diameter. Part of an oviduct was recognizable along one margin of the mass. On section, it was red in the portions which had the appearance of an oviduct. The remainder was yellow, edematous, and had the appearance of an ovarian stroma.

Sections showed decidual reaction and chorionic villi in the dilated lumen of the oviduct. The villi were coarse and quite adult.

Diagnosis: Tubal pregnancy.

CASE 2.—E. R., aged 29 years, married four years, was admitted to the Queens General Hospital November 10, 1936, complaining of a constant sharp pain in the right lower quadrant of the abdomen. Her only pregnancy had terminated in the spontaneous delivery of a full-term child March 1, 1936. Her menses returned in April and were regular, every twenty-eight days, until September 2, the date of her last period. On October 10, she spotted for one hour. November 6 she was seized with sharp, nonradiating pain in the right lower quadrant which on November 10 was so severe that it caused her to faint. There was no nausea or vomiting, but there was slight dysuria. No shoulder pain, no dyschesia, and no vaginal bleeding or discharge.

On admission the general condition of the patient was very poor and she was in obvious shock. The abdomen was tender and rigid, with rebound phenomenon present in the right lower quadrant. There was no shifting dullness and no masses were palpable. Vaginal examination revealed no free bleeding and a uterus the size of an eight to ten weeks' gestation with a soft cervix which was exquisitely tender on motion. A tender doughy mass was present in the right fornix. A blood count at this time showed white blood cells 12,300 (85 per cent polynuclears), red blood cells 3,200,000, hemoglobin 62 per cent. The sedimentation time was thirty-five minutes.

A diagnosis of ruptured ectopic gestation was made and an immediate laparotomy performed. The peritoneal cavity contained about 500 c.c. of dark blood and blood clots. The uterus was soft and the size of a two months' pregnancy. The left tube and both ovaries appeared grossly normal. The right tube was the site of a ruptured ectopic gestation in the ampullary portion. A partial right salpingectomy was performed and the abdomen closed.

The patient was transfused postoperatively, her convalescence was uneventful and she was discharged November 20.

Pathologic Report.—Gross: Specimen consisted of a mass 4 by 5 cm. in diameter, an old blood clot being present near the fimbriated end. *Histologic:* Areas of decidual cells and chorionic villi were seen throughout the tubal mucosa.

Diagnosis: Tubal pregnancy.

On Feb. 2, 1937, the patient was readmitted to the gynecologic service for removal of a small but painful vaginal cyst. At that time the uterus was the size of a four and a half to five months' gestation, and fetal heart sounds were heard in the left lower quadrant. There had been no menses since Sept. 2, 1936. She was discharged Feb. 10, 1937. On May 27, 1937, the patient was admitted to the obstetric ward in active labor, and one hour later delivered a full-term living male weighing seven and a half pounds. The puerperium was uneventful and she was allowed home June 6, 1937.

SUMMARY

Two cases of extrauterine and intrauterine gestation are reported. In the first case, chorionic villi were found, both in the scrapings obtained from uterine curettage and in the tube which was subsequently removed at laparotomy. In the second instance, the intrauterine pregnancy went on to term, despite a laparotomy at the second month for a ruptured ectopic gestation.

I wish to express my appreciation to Dr. Arthur Antony and Dr. Harry P. Mencken for their permission to abstract these records.

106 McDonough Street

SUCCESSFUL TERMINATION OF PREGNANCY FOLLOWING BILATERAL SYMPATHECTOMY*

Joel Miller Melick, A.B., M.D., F.A.C.S., Worcester, Mass.

THE treatment of essential hypertension until a few years ago was entirely medical. In 1923, Danielopolu, Bruening, and Stahl resected splanchnic nerves for this condition. In 1924, Pende proposed resection, and in 1934 Durante of Genoa proposed the same. Adson of the Mayo Clinic in 1925, performed a bilateral lumbar sympathetic ganglionectomy for essential hypertension. This was not successful, but the interest was again stimulated in 1930, after a successful rhizotomy. By October, 1935, twenty-seven patients were operated upon in the Mayo Clinic with different types of nerve resections for this condition. Several others reported a series of such cases as Crile, De Courcys, Page, Heuer, and Peet.

The conclusions of the Mayo Clinic from which the above data were obtained were that "the interval following the surgical procedure is too short to prognosticate what the ultimate results will be." They apparently feel quite hopeful that some form of surgery will eventually help a rather high percentage of well-selected cases.[1]

Among the patients operated upon at the Mayo Clinic only two have subsequently become pregnant. The first patient had previously borne three children, the youngest 6, and with none of the previous pregnancies had she shown signs of toxemia. Extensive sympathectomy was performed with relief of symptoms and reduction of blood pressure. Two years later she became pregnant. For two and a half months she was free from symptoms and her blood pressure was satisfactory. At three and a half months her blood pressure rose to 200/110. Termination was recommended. At five and a half months she was aborted by hysterotomy; her blood pressure was 200/110, and she was dyspneic and vomiting. Twelve weeks later her blood pressure was normal and has remained so for two years.[2]

*Presented at a meeting of the Worcester District of the Massachusetts Medical Society, April 13, 1938.

I wish to report a second case of pregnancy following an extensive sympathectomy.

Mrs. F., age 33 years, was referred to me by Dr. Brosnan of the Fallon Clinic of Worcester. At this time she had missed only one menstrual period, but a positive Aschheim-Zondek test had been obtained. The uterus was enlarged to about a two months' pregnancy. She gave the following menstrual history: began at 13, frequency every 30 days; duration one day; amount scant; no pain and regular every month. Her measurements in centimeters were intercristal 26; interspinous 20; external conjugate 19; bisischial -7, with a narrow arch; diagonal conjugate 13+, but an anteflexed, fused sacrococcygeal articulation. Her past history: diphtheria, chicken pox, whooping cough, mumps, and measles twice in childhood. Pneumonia at 8 and at 30; left nephrolithotomy at the age of 22 for renal stones; at 24 the same kidney was removed on account of infection; at 25 appendectomy; at 29 dilatation and curettage and hemorrhoidectomy; at 31 her blood pressure had gradually risen to 230/110, and she was classified as the essential hypertension type with no signs of damage in the remaining kidney; no evidence of arteriosclerosis or hypertensive heart disease. In 1935, at the Mayo Clinic an extensive bilateral subdiaphragmatic sympathectomy was performed. This included the section of both splanchnic nerves on each side as well as the two upper lumbar ganglia and partial resection of each suprarenal gland. She became pregnant two years later.

Course of the pregnancy: When she first came to me, at about two months, the blood pressure was 120/90 and with no symptoms of headache, faintness, or vertigo. I saw her every three weeks until the sixth month, and then every week until term. Her blood pressure ranged from 120/90 to 175/115. This maximum was reached at the seventh month and then receded to 140/95 at term. At no time did she have any toxic symptoms. Her weight increased from 128½ at the second month to 151 at term. At term her membranes ruptured before labor pains began. She had fourteen hours of first-stage labor and two hours of second-stage labor which was terminated with midforceps. The coccyx was fractured. A living female infant was delivered. She had an uneventful post-partum period. During labor the highest blood pressure was 184/118, and subsequently averaged around 150/110 while in the hospital. Five weeks after delivery her blood pressure was 160/90. Since then her blood pressure has reached as high as 170/105, but at present is 140/90. Although her weight is still around 140, she feels perfectly well and is enjoying the care of a normal healthy baby.

Only two cases of pregnancy following extensive sympathectomy have been reported, as far as I can determine. The first was aborted at five and a half months. The second case, discussed above, was carried through pregnancy to a successful termination. The first case proves that pregnancy following this operation is a definite hazard. The second proves that in spite of this hazard pregnancy can be carried through to a successful termination, but should be watched carefully throughout.

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27 Elm Street

Randall, Lawrence M., and Herrell, Wallace E.: Cystic Changes in the Endometrium, Surg. Gynec. Obst. **65**: 666, 1937.

Microscopic study of 278 specimens of endometrium removed with a biopsy curette revealed that in 28 of them cystic changes had occurred. These tissues represented all phases of the menstrual cycle from the early proliferative phase to the late differentiation. The cystic change is believed to be the result of failure or deficiency of the function of the corpus luteum. The amount of proliferation is dependent on how complete or persistent this failure or deficiency has been.

Wm. C. Henske.

UTEROPLACENTAL APOPLEXY*

J. P. McComb, M.D., Pittsburgh, Pa.

UTEROPLACENTAL apoplexy is a grave complication of pregnancy in which there is marked hemorrhagic infiltration of the uterine wall with dissociation of the individual muscle fibers. The process may also extend to the broad ligaments and to the tubes and ovaries. The condition follows premature separation of the normally implanted placenta.

Couvelaire designates this condition as "uteroplacental apoplexy." Kolisko describes it as "hemorrhagic infarction of the uterus." Gibbon-Fitzgibbon terms it "ante-partum hemorrhage." Batizfalvy calls it, in mild cases of premature separation of the placenta, "ablatio placentae" and in severe cases, "uteroplacental apoplexy." This would seem to me to be a satisfactory nomenclature.

Case 1.—Mrs. A. P., para vi, aged 35 years, American born, Italian parentage; of hypopituitary type; weight 210 pounds; height 5 feet 1 inch, admitted by ambulance, Jan. 21, 1937. Family and past personal histories negative. Menstruation began at the age of thirteen years; the periods were regular, every twenty-eight days, lasted four to five days, and were attended by no pain. She had had one abortion at three months, between the second and third pregnancies. Her five children were living and well. Patient stated that four of the labors were long and difficult. Last period July 21; expected confinement April 28, 1937.

Physical examination was negative except for the presence of dental caries involving several teeth, and edema of the feet which she said she had with each pregnancy.

On the evening of admission to the hospital, without any warning or any sign of pain, she had a profuse hemorrhage. She continued to flow intermittently after being put to rest with ice to her abdomen. When admitted to the hospital by ambulance the bleeding had ceased.

Examination revealed the uterus definitely larger than a 6 months' pregnancy, of firmer consistency than normal, with no pain or contraction. Inability to elicit the fetal heart tone was attributed to the obese abdominal wall. Rectal examination revealed the cervix to be about 1.5 cm. in length, patulous, 2 cm. The presenting part could not be palpated. The blood pressure was 130/70, the pulse 80, the temperature 98.6° F. The hemoglobin was 59 per cent. The patient's condition seemed satisfactory.

The patient and her husband were typed, with blood transfusion in mind, and each was found to be Type II. At this time the patient's pulse had increased to 104, the pressure dropped to 118/65, and the hemoglobin to 39 per cent. The red cell count was found to be 1,990,000, and the urine was found to contain a marked trace of albumin and occasional hyaline casts. The patient was given 400 c.c. of citrated blood by transfusion, following which she slept for three hours.

A vaginal examination was made, when it was found that the placental tissue could not be palpated through the patulous cervix. No fetal heart tone could be elicited. A definite ligneous consistency of the uterus had developed during the past three hours, and vaginal bleeding required change of pads four times since admission.

The diagnosis of ablatio placentae being established, the patient was prepared for laparotomy. Under nitrous oxide and ether anesthesia the abdominal cavity was entered through a suprasymphysial incision; the peritoneum was opened, exposing a uterus markedly injected, red and edematous with infiltration of blood in the uterine wall running at right angles to the axis of the uterus. The uterus seemed

*Read at a meeting of the Pittsburgh Obstetrical Society, June 6, 1938.

to exude serum, and there were several ounces of bloody fluid in the pelvic cavity. We felt that the involvement of the uterus necessitated its removal, and consequently a supracervical amputation of the uterus was performed without section, conserving both tubes and ovaries. The tissues were extremely friable, frequently necessitating duplicate ligatures and suture to control bleeding. The opening into the cervix was closed with inverting suture No. 1 plain catgut, the round ligaments were sutured to the stump of the cervix with No. 1 plain catgut, and the raw area peritonized with suture of the same material. Iodoform drain was enclosed in tissue in the lower angle of the wound extending down to the stump of the cervix, and the abdomen was closed in the same manner.

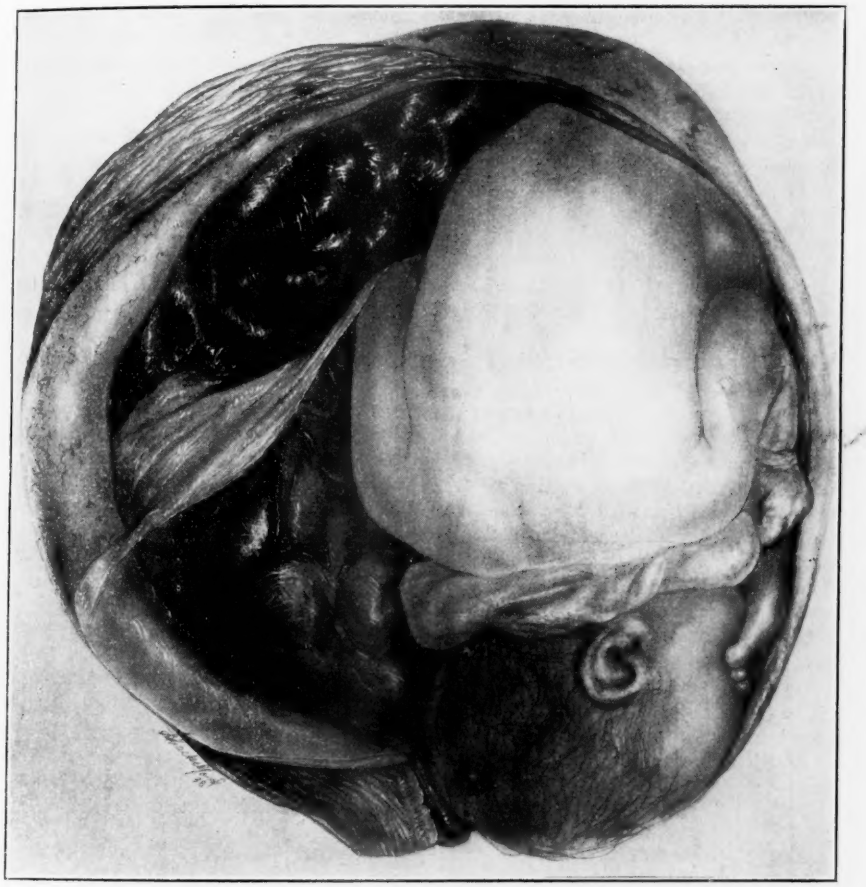

Fig. 1.—Drawing of Case 1, showing uteroplacental apoplexy occurring in upper pole combined with marginal insertion of the placenta.

The immediate postoperative condition was poor. A second transfusion and intravenous glucose proved of marked benefit. During the first four days the temperature went up to 102.2° F. and the pulse to 120; thereafter the patient made a good convalescence and was discharged from the Hospital at the end of nineteen days with slight drainage from the lower angle of the wound.

On opening the uterus there was found a low implantation of the placenta, but the hemorrhage had occurred at its upper pole, involving half its extent. The lower half of the placenta was not disturbed. The cord was shortened by a turn about the baby's neck and seemed to be under tension.

CASE 2.—Mrs. S., para i, aged 33 years, married two years. American born of Polish parentage; weight 159 pounds, height 5 feet 6 inches; admitted by automobile on the night of March 13, 1937. Family history negative. Her past personal history included heart disease at the age of 3 and a spinal injury by automobile accident at the age of 12. Menstruation began at the age of 18, and periods occurred at three-month intervals, lasting four days, moderate in amount with little pain. Last period July 5. There was quickening on November 22; estimated confinement date April 12.

Physical examination was negative. The patient had been observed prenatally on five occasions, and the blood pressure and urine were found to be normal. She developed edema of the ankles which at times was painful. After strapping this disappeared. Her weight increase up to two weeks prior to admission was 25 pounds.

On admission to the hospital the patient complained of abdominal pain which had started two hours earlier and localized over the uterus. The uterus was symmetrical in outline and tense on palpation. Repeated examination failed to elicit the fetal heart tone. Rectal examination showed the cervix about 1.5 cm. long, admitting the examining finger, and cephalic presentation was found.

The patient was given an HMC tablet No. 2 and slept at long intervals through the night. When awake she complained of backache. At 6 A.M. the following morning there was a show of blood, and by 9 A.M. there was a return of abdominal pain. The abdomen again became tense and the patient complained of continuous severe pain. The blood of the patient and of three relatives was typed and found to be Type II. The blood pressure was 114/70; red cell count 3,460,000; hemoglobin 65 per cent.

There was very little change in the cervix on rectal examination, and the patient was prepared for laparotomy.

The abdomen was entered through a suprasymphysial incision. The anterior aspect of the uterus was pallid and tense on palpation. It was opened in the midline, and a dead female fetus delivered by podalic extraction; weight 5½ pounds. The placenta, located high up on the posterior wall, was separated in about one-third of its extent; from behind the placenta, clots approximating a pint were removed. The uterus was delivered from the abdomen. The posterior uterine wall was edematous and infiltrated with blood. Hemorrhagic areas extended to the broad ligament attachment. Bleeding from the uterus was quite free with no tendency to contract after a second injection of pituitrin.

The uterus was amputated at the level of the internal os. The opening of the cervix was closed by an inverting suture, No. 1 plain catgut, and the vessels were ligated with the same material; the round ligaments were sutured into the stump of the cervix and the raw surface peritonized with No. 1 plain suture. The abdominal wound was closed in the usual manner. The postoperative condition was good and transfusion was omitted. The patient made an uneventful recovery and was discharged from the hospital at the end of twelve days.

I would like to thank Drs. Morris, Bruecken, and Rebbeck for technical help with these cases.

TUBERCULOSIS OF CERVIX

HENRY S. FISCHER, B.S., M.D., F.A.C.S., AND DAVID HELD, M.D.,
BROOKLYN, N. Y.

(From the Gynecological Service, Beth Moses Hospital)

JAMESON states that "Tuberculosis of the cervix is considered to be one of the more uncommon localizations of the disease in the female genital tract." Comyns Berkeley in 798 autopsies upon women who died of tuberculosis, found the reproductive tract involved in 62 cases, and of these, but 3 cases of tuberculosis of the cervix alone. Because of its rarity and the attendant problems involved in advising proper treatment in this type of case, the following case report is submitted:

R. I. (No. 81647), white, 19 years of age, Russian, housewife, was admitted to the private service of the senior author on Jan. 4, 1938, with chief complaint of vaginal bleeding occurring only after coitus. She had been married nine months and although staining was the usual aftermath following coitus in the early months of her marriage, this bleeding during the past four months had become markedly profuse. She had used no contraceptive measures and had been extremely anxious to become pregnant.

Her menstrual cycle, which began at the age of 12, at 26-day intervals and lasting three days, had always been of a normal rhythm. No dysmenorrhea, menorrhagia, or metrorrhagia was noted.

Both parents were living and well. Mother had goiter operation five years ago. Six sisters were living and well and all had had one or more children. Intensive questioning elicited no history of tuberculosis, diabetes, or cancer.

Except for tonsillectomy one year ago and measles as a child, patient had always been known as a "healthy" individual, and had no complaints concerning the respiratory, genitourinary, gastrointestinal, or cardiovascular systems.

(The husband of the patient was questioned as to family and personal history with negative results. Physical examination was essentially negative. Examination by a genitourinary specialist was reported as negative as to any possible source of tubercular or venereal infection in the male reproductive system.)

Physical examination of the patient revealed a well-nourished "healthy," white female with essentially negative objective physical findings except for those noted upon vaginal examination. The vulva was negative and presented a nulliparous introitus. Uterus was of normal size, anteverted and anteflexed, freely movable and regular. The fornices and cul-de-sac were negative. The cervix upon inspection appeared slightly hypertrophied, and, about the external os for a radius of about ½ inch, there was present a granular, velvety, angry red, and extremely friable erosion with a well demarcated and "punched out" regular margin. This area bled easily to the slightest touch. A preoperative diagnosis of a cervical erosion with tuberculosis, cancer, and syphilis to be ruled out was made, and trachelorrhaphy and microscopic study advised.

The blood pressure was 115/70; urine, negative; Rosenthal and Kahn, negative; guinea pig inoculation (catheterized specimen of urine), negative.

Blood examination showed hemoglobin, 13 gm.; R.B.C., 4,200,000; W.B.C., 10,000; polymorphonuclears, 81; and lymphocytes, 9.

X-ray Flat Plate of Chest—Summary: Old low grade Koch infection of apices especially the right one. Old hilus tuberculosis. Generalized peribronchitis and hypervascularization. No evidence of cavitation.

Frequent attempts to examine sputum for the tubercle bacilli were unsuccessful due to insufficient amount of expectorated material.

Vaginal, cervical, and urethral smears showed no gram-negative intracellular diplococci.

Under general anesthesia on Jan. 5, 1938, the cervix was coned out with the line of incision extending slightly beyond the demarcated edge of the eroded area. Post-

operative course was uneventful and the patient was discharged eleven days post-operative. Further studies in seeking other foci of tuberculous infection were incomplete, due to lack of cooperation upon the part of the patient who insisted upon leaving the hospital. She was seen two weeks after discharge, the suture line was well healed and the patient had no complaints.

Personal communication with the referring physician (Held) elicits the information that the patient no longer complains of bleeding after coitus, and, to all intents and purposes, feels well.

Pathologic Report.—(Laboratory No. 7358.) *Gross:* Specimen consisted of a conical shaped mass of tissue 1.7 cm. in height, 2.5 cm. in diameter. At the mucocutaneous junction, there was an angry red, granular zone which was completely circumferential. *Microscopic:* The mucosal epithelium was absent from over many

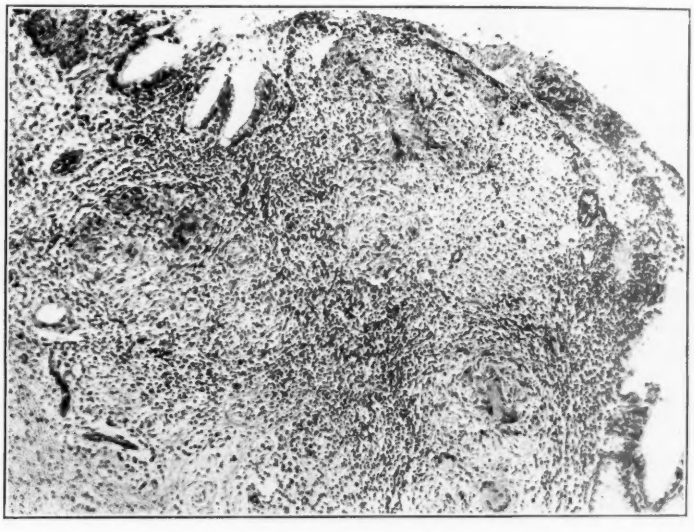

Fig. 1.—Tubercles showing caseation necrosis and Langhans giant cells beneath the surface epithelium.

areas. Exudate with polynuclear and mononuclear cells was adherent to the eroded surface. In the underlying tissue, conglomerations of mononuclear and polynuclear cells, with the former predominating, epithelioid cells and Langhans' giant cells were noted. Areas with necrosis and especially fibrosis formed the central portions of the cellular collections.

Examinations for acid-fast bacilli were negative.

Diagnosis.—Tuberculous endocervicitis.

DISCUSSION AND SUMMARY

It is not within the scope of this case report to discuss the mode of infection, prognosis or treatment of cases of tuberculosis of the cervix. Evaluating the facts in our own case, we were inclined toward a conservative type of therapy. It was primarily our intent to stress the importance of clinical observation and microscopic study in cases which ofttimes are dismissed as simple erosions of the cervix. Although it is estimated that about 75 per cent of the cases of tuberculosis of the cervix have involvement higher up in the genital tract, a case of a possible (since no laparotomy or curettage was performed) primary tuberculosis of the cervix is presented in an apparently healthy young woman.

789 St. Marks Avenue
1579 Sterling Place

PREGNANCY COMPLICATED WITH BILATERAL CYSTIC OVARIES

C. D. HOFFMANN, M.D., F.A.C.S., ORLANDO, FLA.

IN THE June issue of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, there appeared an article by Dr. Bernard Notes of Washington, D. C., relative to a bilateral oophorectomy done during the early months of a pregnancy, the pregnancy continuing on through to near term without interruption.

The following case I have to report is rather unique in the fact that the patient not only continued through to term, but two years later became pregnant from a very small stub of ovarian tissue and carried through to term again.

L. A. (Hospital No. 4017), white, aged 27 years, admitted to Orange General Hospital, Orlando, Fla., Oct. 29, 1935. The chief complaint on admittance was heavy, dull, dragging, constant pain in the left lower quadrant of the abdomen for the past two weeks. Past history other than the menstrual history was insignificant. Menstruation began at age of 14 years, regular every twenty-eight days, flow four to five days until after birth of first child, when occasionally she would skip one month. Pregnancies were as follows: Full-term normal delivery 1931 and 1935. One miscarriage at three months in 1934. Received six milk injections following this miscarriage. The second child born in 1935 was seven months old when the patient was admitted to the hospital, this child being breast fed. Patient stated that she had had only three periods since birth of child in April, 1935, the last period being Sept. 12, 1935, when she flowed three days, but since she was nursing her baby she was not alarmed over the irregularity of her periods.

The laboratory examinations were within normal limits and the Kahn test negative. Pelvic examination: Marital outlet with moderate relaxation of the perineum. Small amount of mucopurulent discharge. Cervix showed very slight erosion of the external os, but no laceration. Uterus was apparently not enlarged but was pushed to the left. There was a marked fullness in the left fornix which was soft, tender, and bulging. The right tube and ovary were not felt. A diagnosis of left cystic, ovary was made.

On Oct. 31, 1935, the patient was operated upon through a low midline incision under gas-oxygen-ether anesthesia. On opening the abdomen through a midline incision, the pelvis and culdesac were found to be completely and entirely filled with large bilateral cystic ovaries. The left ovarian cyst was the size of a large grapefruit and was contained entirely within the leaves of the left broad ligament. The right ovary was the size of a large orange, with apparent complete destruction of the ovarian substance. Both ovaries appeared to be nothing but large cystic sacs. The tubes were normal with the exception of a small cyst of Morgagni on the fimbria of the left tube. The uterus was soft and boggy and apparently two to two and one-half months' pregnant.

The operative technique was as follows: Dissection of the left intraligamentary cystic ovary intact, the leaves of the broad ligament being closed with No. 1 plain catgut. The right ovarian cyst was clamped and removed in the usual manner, the base being sutured with chromic catgut. The cyst was removed from the fimbria of the left tube and the appendix was not disturbed.

The specimen consisted of two large cystic masses, both intact and containing serous clear fluid. In the base of the right ovary, inside the cyst wall, was a large corpus luteum. Section of ovary showed large corpus luteum. No evidence of malignancy. Section of cyst wall showed many thin-walled venous sinuses and

considerable number of new fibroblasts. Lining of cyst was smooth. There was no evidence of malignancy. Diagnosis: Simple serous cystic ovaries, corpus luteum of pregnancy.

The postoperative course of this patient was entirely uneventful, and she was dismissed on Nov. 14, 1935, on her fifteenth postoperative day. At no time during her postoperative stay in the hospital did she receive any hormone therapy and received none during her prenatal period. She delivered a full-term, seven-and-three-quarter-pound baby on June 27, 1936.

This patient continued to have very irregular periods, at five- to eight-week intervals, after the birth of this baby, became pregnant again in 1937 and delivered a full-term baby on May 4, 1938.

There are two peculiar aspects of this case: First, the patient carried through to term after removal of the corpus luteum which was completely inclosed in the base of cystic ovary, and second, a subsequent pregnancy with only a very small stub of an ovary left.

NOTE: This patient presented symptoms referable to a complicated retroversion after her delivery in May, 1938, and was operated upon again on Aug. 10, 1938. A small piece of ovarian tissue was found at the site of the large intraligamentary cyst removed in 1935. This was completely subperitoneal and firmly bound down on the posterior surface of the left broad ligament, yet it was the source of another full-term pregnancy in 1938.

A REPORT OF A CASE OF INTRAUTERINE ASPHYXIA OF THE FETUS AT TERM DUE TO A TRUE KNOT IN THE CORD

G. A. MITCHELL, M.D., ST. LOUIS, MO.

(From the Department of Obstetrics and Gynecology, St. Louis University School of Medicine)

BROWNE, King, and others have reported cases of intrauterine asphyxia of the fetus due to a true knot in the cord and have suggested such cases be recorded in the literature. A report of one case is herewith submitted in which this complication caused the death of the fetus at term.

The occurrence of a true knot in the cord according to Williams is very frequent while Von Winckell estimates its occurrence as 0.4 to 0.5 per cent of all births. However, most writers consider death of the fetus, due to a true knot in the cord, as being of rare incidence and many authorities think that this condition is not possible. However, Browne has shown by experimentation that a knot in the cord can be sufficiently tight to occlude circulation of blood through the cord.

The patient, a white multipara, aged 29, para iv, presented herself to the Out-Patient Obstetrical Clinic for the first time on Oct. 1, 1937. The examination was negative with the exception of a mild cervicitis, second degree cystocele and rectocele. The Wassermann, Kahn and Kline tests were negative. The urinalysis was negative. The last menstrual period, which was normal, occurred on July 20, 1937, with expected date of confinement on Apr. 27, 1938. The patient did only the ordinary housework during the pregnancy. The ante-partum course was normal. There was a total weight gain of 23 pounds during the pregnancy. On Apr. 27, 1938, the estimated date of confinement, the McDonald measurement was 33 cm., head floating, fetal heart rate 136/min., rectal or vaginal examination was not made.

Upon abdominal examination on May 11, 1938, the McDonald was 34 cm., head entering the pelvis, fetal heart rate 132/min., L.O.A. position; there were active fetal movements. Ten hours later the patient noted the fetal movements were unusually active, but early the next day, May 12, she noted there were no further fetal movements. She returned to the clinic on May 14, at which time the McDonald was 34 cm., no fetal heart tones heard, no fetal movements perceived, and the head

on palpation seemed softer than normal. A clinical diagnosis of dead fetus was made. An x-ray examination of the abdomen showed no evidence of a dead fetus. On May 16, the patient went into labor and four hours later delivered spontaneously a dead macerated child. The umbilical cord was not entangled about the fetus. The cord measured 82 cm. in length; there was an average amount of amniotic fluid. There was a true tightly drawn knot in the cord at a point 54 cm. from the placenta. The cord from the knot to the placenta was a dark red due to hemorrhage and the blood vessels were thrombosed. For a distance of approximately 14 cm. from the knot toward the fetus the cord likewise was hemorrhagic with thrombosed vessels.

This evidence of a true tightly drawn knot in the cord was the basis for the diagnosis of intrauterine asphyxia with resultant death of the fetus at term.

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A SIMPLE AND INEXPENSIVE CARRIER FOR PREMATURE BABIES

BEATRICE MCKELLAR, R.N., BALTIMORE, MD.

(From the Department of Obstetrics, Johns Hopkins Hospital)

IT IS generally recognized that some form of heated carrier is desirable for transporting premature infants from the home to the hospital. In designing such a carrier for our Home Delivery Service three ends were sought: first, the heating system should be safe and simple to prepare; second, the size and weight of the carrier should be no greater than one person could easily transport; and third, the carrier should be inexpensive. The first objective was realized by using hot water bottles for providing the heat; the second by the choice of a black leather composition animal carrier which could be altered according to our special needs. The total cost of the carrier amounted to approximately eight dollars; the animal carrier cost four dollars, the three hot water bottles three dollars, and other materials not more than one dollar. This represents a considerable saving since a premature carrier of the type usually shown on the market costs from fifty to one hundred dollars.

The bag chosen was a light weight animal carrier which measured 10 inches deep, 11 inches wide, and 20 inches long. This type bag is easily transformed into a baby carrier as the lid is built like the roof of a house, thus giving an extra five inch clearance above the baby. It has a hole 7/8 inch in diameter at either end of the top as well as an opening 4½ by 5 inches at one end of the box part. The latter is protected by a wire netting over which a leather flap can be fastened. These openings provide for sufficient circulation of fresh air when the top is closed.

A wooden frame was built to fit inside the bag. This was designed to resemble a four-poster bed with the springs represented by a wooden floor raised 3 inches from the bottom of the bag to provide space for one hot water bottle. Holes ½ inch in diameter and 2½ inches apart were bored through the floor to permit the heat from the bottle to reach the baby. The four corner posts were connected to each other at the top by wooden bars. Over the bar on each long side a piece of soft woolen blanket was fastened and then redoubled on itself to form a pocket into which a hot water bottle could be inserted. These pockets were fixed in position by tacking the lower borders to the floor of the frame. The small ends of the frame were not lined. A premature jacket, a pad for the bed, and a small blanket completed the equipment. An opening 4¼ inches square was cut in the top of the carrier and an isinglass window inserted so that the baby can be under constant observation while being transferred to the hospital. Fig. 1 shows the bag.

Wishing to test the efficacy of the heating system the following experiment was conducted. The three hot water bottles were filled with water at 108°; the bag was opened in a room the temperature of which was 56°. A thermometer was placed in the bag, the bag closed and left in the room by an open window with cold air blowing on it. In fifteen minutes the temperature in the bag had risen to 76°.

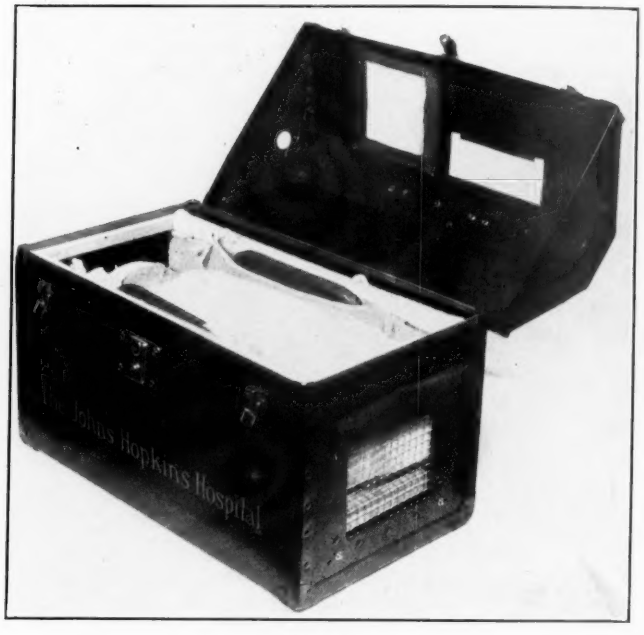

Fig. 1.

On transferring the bag to a warmer room of 78° the temperature rose to 85° within an hour, a greater length of time than the baby would remain in the bag. Therefore, the temperature at which the hot water bottles should be filled was set at not more than 110°. A thermometer was placed in the bag to be used for testing water in the home if necessary.

In our experience, this bag has proved a simple, inexpensive, and efficient means of maintaining the body temperature of premature infants while transporting them to the hospital.

Daniel, C., and Goldenberg-Bayler, S.: Vaccinotherapy in Metrorrhagic Adnexitis, Rev. franç. de gynéc. et d'obst. 33: 1, 1938.

Inflammatory adnexa are the cause of profuse uterine bleeding in 8 to 10 per cent of the cases. In the case of metrorrhagia where the customary treatment does not produce a cessation of the uterine bleeding, it is important to look for inflamed adnexa. The authors believe that vaccinotherapy is the treatment of choice. Not only is it superior to other forms of therapy, but it may be used as a diagnostic measure as well. Thus in a case where it is impossible to differentiate inflamed adnexa from an ectopic pregnancy, if the use of vaccinotherapy is followed by a diminution in size of the mass or even a cessation of the uterine bleeding, the mass is inflammatory and not a tubal pregnancy.

J. P. GREENHILL.

UMBILICAL CORD CLAMP

MILO R. WHITE, A.B., M.D., DETROIT, MICH.

(From the Department of Obstetrics and Gynecology, Henry Ford Hospital)

AN UMBILICAL cord clamp is presented which may be easily sterilized and readily applied and removed. The constricting action of the clamp around the cord insures positive hemostasis regardless of changes in its size.

The clamp, which is illustrated in Fig. 1, is made of 3/16 inch tempered German silver and measures two inches in length. It comprises a spring loop carrying two spring arms. One spring arm is a single strand of wire, except at its free end where it is turned back upon itself to form a finger hold. The other spring arm comprises two parallel portions, between which the first mentioned arm moves. The spring arms

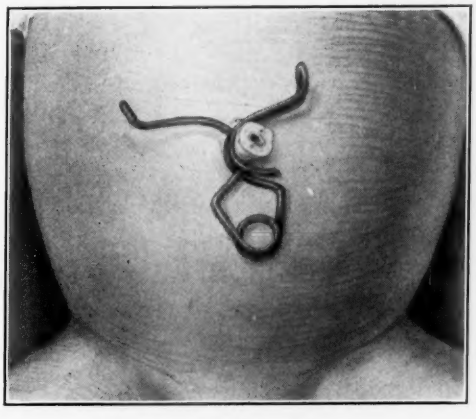

Fig. 1.

have opposing concave portions, which produce a constricting pressure on the entire circumference of the cord. The single strand spring arm tends to pull the cord into the space between the parallel portions of the other spring arm, which precludes the possibility of the clamp being accidentally pulled off.

The clamp is applied by approximating the free ends of the spring arms with the thumb and the index finger. The cord is then drawn through the circular opening formed by the concave portions of the spring arms. The cord is cut ½ inch distal to the clamp. The spring action of the clamp continues until the spring arms come to the position shown in Fig. 2. This insures adequate pressure on the cord even though there may be a decrease in the size of the cord due to the loss of Wharton's jelly.

After twelve to twenty-four hours the vessels are thrombosed and the cord dehydrated so that the clamp may be removed. Early removal of the clamp insures better healing of the umbilicus, because there is no possibility of traction on the cord and its premature separation.

HENRY FORD HOSPITAL

Editorial

Tuberculosis and Pregnancy

THE chance occurrence of pregnancy in a tuberculous woman is frequently looked upon as an unfortunate, if not dangerous, complication. The opinion still prevails among many physicians that abortion is essential to conserve the life of the patient. However, advancement in the treatment of pulmonary tuberculosis in particular has brought about a modification of this radical attitude and hopelessness need no longer prevail among women thus afflicted.

Of interest in this connection is a proposal presented at a recent meeting of the State Charities Aid Association of New York by Dr. Marian F. Loew, assistant director of the Division of Maternity, Infancy and Child Hygiene of the New York State Department of Health. After presenting evidence gleaned from a rather superficial review of the literature purporting to show the deleterious effects of pregnancy on the tuberculous woman, Dr. Loew outlined a plan being considered by the New York State Department of Health whereby an x-ray study would be made of every woman attending ante-partum consultations throughout the State, with a view of throwing "considerable light on the true incidence of tuberculosis in this group" and yielding "an estimate of administrative costs of including an x-ray as part of every ante-partum examination."

While the importance of recognizing a tuberculous lesion in a pregnant woman early in the course of gestation cannot be disputed, there are a number of points raised by Dr. Loew's proposal that are open to serious question. The evidence provided by a similar survey of 1,073 cases x-rayed by the Bellevue-Yorkville Health Demonstration in New York City in 1933 and 1934 and Bridgeman and Norwood's study of 14,000 patients at the Johns Hopkins Hospital, indicate that the incidence of tuberculosis in pregnancy approximates that of the population as a whole. This being so, as expensive a method of case finding as routine x-rays of the chest would seem to be unwarranted by a state health department even as a research problem. It should also be pointed out that the results of a study so conducted would fail to answer the question of the incidence of tuberculosis in pregnancy except as applied to the rather special low-income group of patients who would be seen in the State-conducted prenatal clinics.

In addition to these criticisms of the plan, Dr. Loew's proposal to defer the examination until the fifth month of pregnancy or even later "to secure a true picture of the lung findings" would do much to nullify the practical value of the study. It is now rather generally agreed that

if a gestation in a tuberculous woman is to be interrupted, the uterus should be emptied not later than the twelfth week, and if the pregnancy is to be allowed to continue, the patient should be well started on a tuberculosis regime by the fifth month.

Of much more practical importance than the proposed study would be efforts to provide adequate tuberculosis and obstetric care for pregnant patients with phthisis. At the present time facilities are almost entirely lacking, not only in New York State but also, with one or two exceptions, in other states as well for the care of the tuberculous gravid woman through the antenatal period, parturition, and puerperium. This being so, the deleterious effects of pregnancy on pulmonary tuberculosis must be attributed primarily to lack of proper treatment of the lung disease and secondarily, if at all, to the pregnancy itself.

Edwin M. Jameson, M.D.

Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

CESAREAN SECTION

AN ANALYSIS OF 1,000 CONSECUTIVE OPERATIONS

EDWIN F. DAILY, M.D., WASHINGTON, D. C.

(From the Department of Obstetrics and Gynecology, University of Chicago)

INCIDENCE

THE cases analyzed in this paper are 1,000 consecutive cesarean sections performed since the affiliation of the Chicago Lying-in Hospital with the University of Chicago, in the service of Dr. Fred L. Adair. The period covered by the study is from May, 1931, to March, 1938. There were 18,009 patients delivered in the hospital during this period, giving an incidence of cesarean sections among hospital cases of 5.5 per cent.

There were 50 operators for the entire series, 28 of whom were residents or full-time members of the departmental faculty and 22 were physicians in private practice. The departmental staff operated upon 79.2 per cent of the cases, the courtesy staff upon 20.8 per cent. No one man operated upon more than 8.2 per cent of the 1,000 cases.

Types of Operations.—

527	Laparotrachelotomies	52.7 per cent
399	Laparotrachelotomies and sterilization	39.9 per cent
59	Porro cesarean section	5.9 per cent
14	Classical cesarean section (7 sterilized)	1.4 per cent
1	Vaginal cesarean section	0.1 per cent

Sterilizations.—

465	of the patients were sterilized	46.5 per cent
	287 by Madlener technique	
	119 by resection of tubes (Adair technique)	
	59 by Porro cesarean section	

Maternal Mortality.—

There were a total of 8 deaths following the operations, a percentage of 0.8.

Two patients died of tuberculous meningitis, the operations being performed ante mortem to obtain a living child.

One patient, a decompensated cardiac case with chronic nephritis, died of cardiac failure following a classical cesarean section.

One death resulted from postoperative abdominal hemorrhage, from a bleeding omental vessel, the operation, a laparotrachelotomy, being performed because of a contracted pelvis and a previous cesarean section.

One death, 78 days postoperative, was the result of generalized infection; the patient had a history of chronic endocarditis. The laparotrachelotomy and sterilization was performed because of a mitral stenosis.

One death was from bilateral pulmonary embolism following thrombophlebitis. The laparotrachelotomy was done for placenta previa.

One patient died of generalized peritonitis following a Porro cesarean section performed after the membranes had been ruptured, the patient in labor over twenty hours. The indication was cephalopelvic disproportion.

One patient died of generalized peritonitis following a laparotrachelotomy combined with a myomectomy and left salpingo-oophorectomy. The indication for operation was fibromyomas of the uterus.

Morbidity.—The standard as advocated by the American Committee on Maternal Welfare was used in calculating the morbidity of these patients. Any patient with a temperature of 38° C.(100.4° F.) or over, recorded on any two days after the first twenty-four hours post partum, oral temperature readings being made at least four times daily, is regarded as febrile.

There were 438, or 43.8 per cent, of the 1,000 patients who became febrile according to the above standard and 122 who remained in the hospital longer than fourteen days postoperative. Of the 527 patients having a laparotrachelotomy without sterilization, 45.7 per cent became febrile. Of the 399 patients having a laparotrachelotomy and sterilization, 40.0 per cent became febrile. The lower morbidity in the sterilization group is probably explained by the fact that these operations are more frequently elective. Of the 59 patients having Porro cesarean sections, 59.5 per cent became febrile. Of the 14 patients having a classical cesarean section, 85.7 per cent became febrile. The one vaginal cesarean section was febrile.

Influence of Labor on Morbidity: Of the 1,000 patients, 334, or 33.4 per cent, were in labor at time of operation; 50.7 per cent of these patients became febrile. 173 patients were in labor twelve hours or more; 54.3 per cent became febrile. 161 patients were in labor less than twelve hours; 49.0 per cent became febrile. 666 patients were *not* in labor; 40.4 per cent became febrile.

Influence of Ruptured Membranes on Morbidity: Of the 1,000 patients, 207, or 20.7 per cent, had ruptured membranes at the time of operation; 113 or 54.6 per cent became febrile. 106 patients had ruptured membranes for twelve hours or more; 61 or 57.5 per cent became febrile. 101 patients had ruptured membranes for less than twelve hours; 53 or 52.5 per cent became febrile. 793 did *not* have ruptured membranes; 40.9 per cent became febrile.

Fetal Mortality.—There were 24 stillbirths, 17 of which were premature births (weighing less than 2,500 gm.). Abruptio placentae preceded 21 of these, placenta previa 2, and eclampsia 1. Forty-three infants, of which *27 were premature births,* died in the neonatal period. A total of 67, or 6.7 per cent, of the infants were stillborn or died in the neonatal period; 44 were premature and the majority of the deaths followed abruptio placentae or placenta previa.

Indications for Operation.—Many patients presented multiple indications for operations so that it was necessary to classify them according to the major factor in making the decision for operation in each case.

Disproportion and Dystocia: Contracted pelvis, 333; dystocia dystrophy syndrome, 41; cephalopelvic disproportion, 27; prolonged labor with inertia, 13; cervical dystocia, 21; Bandl's ring, 2; previous Dührssens incisions, 2; previous third tear recently repaired, 4; plastic repair of urethra, 1; atresia of vagina, 3; vaginal and vulval varices, 1; previous difficult labors with repeated stillbirths, 8; elderly primiparas, 7; fibromyomas of uterus, 13; transverse, brow or face, 7; 48.3 per cent.

Hemorrhage: Placenta previa, 79; abruptio placentae, 46; 12.5 per cent.

Toxemias and Related Conditions: Chronic nephritis, 42; pre-eclampsia (nonconvulsive), 65; eclampsia (convulsive), 9; essential hypertension, 7; 12.3 per cent.

Previous Cesarean Section: No other indication other than sterilization or threatened rupture of uterine scar, 118; 11.8 per cent.

Cardiac Disease: 104; 10.4 per cent.

Other Chronic Organic Disease and Certain Local Complications: Umbilical or ventral hernia, 9; diabetes, 9; pulmonary tuberculosis, 9; tuberculous meningitis, 2; tuberculosis of hip, 1; thrombocytopenic purpura, 2; twisted ovarian cyst, 2; right hydronephrosis, 2; 1 kidney, 1; Gaucher's disease, 1; other indication for sterilization, 4; carcinoma of cervix, 2; acute cholecystitis, 1; brain tumor, 1; multiple sclerosis, 1; 4.7 per cent.

Previous Cesarean Sections.—279, or 27.9 per cent, of the patients had a previous cesarean section. 233, or 23.3 per cent, had one; 42, or 4.2 per cent, had two, and 4, or 0.4 per cent, had three previous cesarean sections. Of the 279 patients who had previous cesarean sections, 207, or 74.9 per cent, were sterilized. 167, or 71.6 per cent, of the 233 patients who had one previous section, were sterilized. 37, or 88.1 per cent, of the 42 patients who had two previous sections, were sterilized. 4, or 100.0 per cent, of the 4 patients who had three previous sections, were sterilized.

Previous Stillbirths.—Of the 563 women who had previously borne children, 113, or 20.0 per cent, had had stillbirths. The majority of the previous stillbirths resulted from prolonged labors or difficult instrumental deliveries. The indication for the cesarean section in most of these cases was contracted pelvis, but in a few cases cesarean sections were performed because of the history of previous difficult deliveries with resultant stillbirths.

Period of Gestation.—9.9 per cent were from 41 to 44 weeks, 46.1 per cent were in the fortieth week, 36.4 per cent were 36 or more but less than 40 weeks, and 7.5 per cent were 26 or more but less than 36 weeks. The operations performed before the thirty-sixth week of gestation were almost entirely upon patients having abruptio placentae, placenta previa, chronic nephritis, or severe toxemia failing to respond to conservative treatment.

Anesthesia.—Local anesthesia alone, 610 cases, 61.0 per cent; local anesthesia and ethylene, 138 cases, 13.8 per cent; local anesthesia, ethylene and ether, 21 cases, 2.1 per cent; local anesthesia and avertin, 5 cases, 0.5 per cent; local anesthesia and cyclopropane, 4 cases, 0.4 per cent; ethylene, 98 cases, 9.8 per cent; ethylene and ether, 106 cases, 10.6 per cent; cyclopropane, 17 per cent, 1.7 per cent; ether, 1 case, 0.1 per cent.

The anesthetic of choice is novocaine, 0.5 per cent used for local infiltration. Ethylene is used to supplement the local anesthesia when necessary. Some patients in labor are difficult to control under local anesthesia and ethylene or cyclopropane is the initial anesthetic. Ether is only added when ethylene fails to relax the patient sufficiently.

SUMMARY

The comparison of the analysis of the first 500 operations with the second 500 operations shows certain significant differences.

The percentage of patients sterilized at time of operation increased 15 per cent. This increase is probably explained by the increased number of operations performed because of cardiac or other chronic organic diseases.

The use of the Madlener technique for sterilization increased 56 per cent while resection of the tube technique decreased 40 per cent.

The maternal mortality decreased 40 per cent (5 to 3).

The morbidity decreased 11 per cent.

The number of operations performed because of contracted pelvis decreased 33.2 per cent, for pre-eclampsia decreased 52 per cent, and for eclampsia decreased 85 per cent, while the operations performed because of previous cesarean section (no indication other than sterilization) increased 103 per cent, for cardiac disease increased 97 per cent, and for chronic nephritis an increase of 143 per cent.

Cesarean section is considered definitely contraindicated when a patient has a convulsive toxemia. Operations upon eclamptic patients are only performed when other indications for the operation are present and after the convulsions have been controlled by conservative treatment. There was only one operation performed on a patient with eclampsia in the second series of 500 operations. Cesarean section is performed on pre-eclamptic patients only when improvement has not occurred under conservative treatment.

The low mortality rate for these 1,000 operations has only been made possible by a combination of factors not readily available in smaller cities and rural areas. Most of the patients had attended the prenatal clinic throughout their pregnancies. Patients with cardiac disease, diabetes, tuberculosis, syphilis, toxemia, etc., are given special attention in designated clinics.

The hospital was built and equipped to provide every possible safeguard to the health of maternity patients. There is complete isolation of all infected mothers and infants from the other patients. Facilities are available for immediate transfusion of blood at any time.

Every patient in the hospital is seen by a senior staff obstetrician at least once a day and by the resident staff more frequently. No major operation is decided upon without consultation with the senior staff obstetrician and no operation is performed by a resident without assistance from a member of the departmental staff. Local anesthesia is the anesthetic of choice and without question the safest for this type of operation.

CONCLUSIONS

These cases have not been analyzed with the idea of minimizing the risk of cesarean section but rather to point out that when the operation is indicated, performed at the proper time, in a suitable hospital by a competent obstetrician, the mortality rate is consistently low. It is the ill-advised, ill-timed operations performed by unskilled obstetricians or surgeons in hospitals not equipped to safely care for maternity patients that have brought discredit upon the operation in many communities today.

Equally as good results are obtained in similarly organized and administered institutions and can be made possible in other hospitals. The requirements of the American College of Surgeons for approval of hospitals accepting obstetric patients should be rigidly met in every hospital.

Wilson, William: Treatment of Pruritus Vulvae by Alcohol Injections, J. A. M. A. 110: 493, 1938.

Forty-nine cases of pruritus vulvae which had been treated unsuccessfully by various conservative methods and were of long standing (average over eight years) were subjected to subcutaneous injections of 95 per cent alcohol. The needle is inserted perpendicularly through the skin. Only from 2 to 4 minims of alcohol is injected at a single insertion of the needle. The number and spacing of injections depend on the extent of the pruritus, the age of the patient, and the condition of the peripheral circulation. When the circulation seems unimpaired one may inject as much as 4 minims of alcohol beneath every square centimeter of the pruritic skin. General anesthesia was always employed.

Immediately after injection the labial folds, particularly the labia majora, become more or less edematous, reaching a maximum in from twelve to twenty-four hours. After twenty-four hours the edema slowly subsides, so that in from three to ten days the vulva usually appears normal, except for some induration.

The itching usually stops at once. If certain areas are overlooked or improperly treated, these can be reinjected under local anesthesia.

Few patients have complained of pain after alcohol injections. At first the swollen labia are slightly tender to firm pressure; this may persist until the swelling is gone. Some have been slightly annoyed by the numbness which naturally follows degeneration of nerves. Convalescence amounts to no more than a recovery from anesthesia. Some patients resumed their occupation after just one day.

Complications occurred in only two patients; small hematomas developed and were incised.

The results were as follows: 25 patients (51 per cent) had complete relief; 4 experienced partial relief; only 2 had no relief.

There have been 13 recurrences (26 per cent); 5 of these patients had a leucoplakic vulvitis.

GROVER LIESE.

Society Transactions

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF MARCH 3, 1938

The following case report was presented:

Uncontrollable Postpartum Hemorrhage. Drs. J. H. Sharkey, J. B. Montgomery, and J. L. Richards.

The papers of the evening were as follows:

Post-partum Hemorrhage as a Cause of Death. Dr. C. T. Beecham. (For original article, see page 258.)

The Treatment of Myomata Uteri. Dr. J. P. Lewis.

Neonatal Mortality at the Philadelphia Lying-in Hospital. Dr. R. M. Tyson. (For original article, see page 241.)

WASHINGTON GYNECOLOGICAL SOCIETY

MEETING OF JANUARY 22, 1938

The following papers were presented:

Endocrine Treatment for Sterility in the Female. Dr. E. W. Titus.

The Surgical Management of Uterine Prolapse and Associated Benign Pathology. Dr. E. H. Richardson.

MEETING OF MARCH 26, 1938

The following papers were presented:

Roentgen Diagnosis of Pregnancy. A Review. Drs. Joseph F. Elward and Joseph F. Belair.

Etiologic Factors in Sterility. Dr. J. Kotz and Dr. Elizabeth Parker. (For original article, see page 233.)

PITTSBURGH OBSTETRICAL SOCIETY

MEETING OF JUNE 6, 1938

The following case report was presented:

Uteroplacental Apoplexy. Dr. J. P. McComb. (For original article, see page 336.)

Paper of the evening:

An Evaluation of Obstetric Analgesics and Anesthetics. Dr. C. K. Murray.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

Endocrinology

(Continued from January issue.)

Béclère, C.: Treatment of Postmenopausal Trophic Vulvar Disturbances, Bull. Soc. d'obst. et de gynéc. **26**: 378, 1937.

For trophic vulvar disturbances such as atrophy, sclerosis, dryness, and pain Béclère recommends the use of ovarian hormones. He gives intramuscular injections of 10,000 units of estrogenic substance every fifteen days. This is continued until relief is obtained, then the injections are given once a month. In addition to this medication the patients are given local diathermy treatments, to improve pelvic and vulvar circulation and to intensify nutritional exchange. Further therapy consists of the local application of estrogenic substance to the affected vulvar tissue. This combination of therapy has given excellent and remarkably rapid results. The first symptoms which disappear are pain and dryness of the mucosa. Then the vulvar shrinking disappears and coitus again becomes possible. In the author's cases cure was obtained in two months.

J. P. GREENHILL.

Moricard, R.: Clinical Signs of Absence of Folliculin—Atrophy of the Labia Minora, Bull. Soc. d'obst. et de gynéc. **25**: 526, 1936.

In women of menstruating age the labia minora are of variable size and they contain sebaceous glands. When follicular action disappears, there is a progressive decrease in size of the labia minora and a partial disappearance of the sebaceous glands. The labia then become glistening and smooth. Such a condition is observed a few months after castration. The retrogression of the labia minora may be asymmetrical. The author was able to restore the atrophic labia partially to their original state in one case by administering estrogenic hormone.

J. P. GREENHILL.

Palmer: The Schiller Test After the Menopause. Its Use in the Diagnosis of the Absence of Follicular Secretion, Bull. Soc. d'obst. et de gynéc. **26**: 45, 1937.

The Schiller test depends upon the demonstration of the presence of glycogen in the squamous epithelium of the cervix by the addition of Lugol's solution. Palmer has used this test routinely during the past eighteen months, and he can confirm the claims made for the test, namely that glycogen is absent in carcinomatous cells. The present study was carried out on 42 women of whom 17 were in a spontaneous menopause, 19 in a menopause following operation and 6 in a menopause following radiation therapy. The author found that after the menopause glycogen disappeared from the squamous epithelium. In menopausal cases, staining with Lugol's solution produced a drab color in the areas free of glycogen. Conversely if Lugol's solution produces the normal dark discoloration more than three years after a hysterectomy or more than twelve years after a spontaneous menopause there is proved a persistence of follicular secretion. The cause for this persistence should be investigated.

J. P. GREENHILL.

Wiesbader, Jans, and Kurzrok, Raphael: The Menopause, Endocrinology 23: 38, 1938.

Two hundred patients were successfully treated for menopausal symptoms by means of estrogens, an ether-alcohol extract of the whole ovary, and calcium. The best results were obtained in patients in whom menstruation had ceased completely. Uterine bleeding (not menstruation) may result from such treatment. The significance of this is discussed.

J. THORNWELL WITHERSPOON.

Donald, H. R.: Treatment of the Female Climacteric by Follicular Hormone, Brit. M. J. 2: 899, 1937.

The climacteric is associated with a decline in secretory activity of the ovary, and a rise in gonadotropic secretion of the pituitary.

The duration of menopausal symptoms is subject to as much individual variation as their severity and origin. Mild menopausal psychoses—irritability, depression, loss of confidence and mental exhaustion—appear to be benefited by small doses of estrin (3,000 international units, or 0.3 mg. estrone by mouth daily). Vascular spasm with hypertension and edema also responds favorably to estrin therapy. The author employed intramuscular and oral doses temporarily, followed by oral administration alone for a longer period.

The wide range of rheumatic manifestations which characterize the climacteric may also have a vascular origin. Comparatively large amounts of estrin are required over a period of at least six months to benefit these patients. Visceral spasm and functional disturbances of the gastrointestinal tract respond to estrin therapy. No improvement was noted in cases of menopausal asthma and bronchitis. Low backache is difficult to relieve. Additional administration of corpus luteum may benefit the latter.

The dosage varies widely in individuals. Mild cases may require 1,000 international units three times daily by mouth to control symptoms. In severer cases 1 mg. estrone (10,000 I.U.) intramuscularly in oil twice weekly combined with 0.1 mg. (1,000 I.U.) three times daily by mouth may be necessary. Some required higher doses for an initial period of treatment. The vaginal smear test of Papanicolaou is an aid in deciding dosage. The duration of treatment varies in individuals. Reduction in dose must be effected gradually and over a long period of time, beginning at least two months after the patient has been symptom-free.

The question of cost is a vital factor to patient and hospital. It appears illogical for any hospital to deny its patients the established benefits of estrin therapy while permitting expenditure of equal sums of money in the care of many less sinister conditions. The ingenuity of the organic chemist may in the near future provide the answer to the cost problem.

F. L. ADAIR AND S. A. PEARL.

Israel, Leon S.: Evaluation of Endocrine Therapy in Primary Dysmenorrhea, J. A. M. A. 106: 1698, 1937.

Thirteen of the 39 patients were treated with estrogenic substance in the form of hydroxyestrin benzoate (Progynon-B) administered intramuscularly in doses of 5,000 to 10,000 rat units every fourth day for from three to four months. Of this group, six were entirely free from pain only while the substance was administered and four remained symptom free from two to four months following withdrawal of treatment. The remaining three patients were unaffected by the treatment.

Ten patients received antuitrin-S subcutaneously every other day in doses of 200 rat units (2 c.c.) for periods of from two to three months. Four patients experienced relief from dysmenorrhea: one has remained well for a period of fourteen months after the withdrawal of treatment, and the other 3 had painless periods during the course of the treatment only. The remaining 6 patients were unaffected by the treatment.

Sixteen patients were given small oral doses of estrogenic substance; 10 of these received emmenin in doses of 1 tablespoonful three times daily for periods averaging four months. Three of these were relieved of pain; one has remained symptom free for one year following the course of the treatment, and the other two only while emmenin was administered. The remaining 7 patients were unaffected. Six of the patients were given progynon tablets in doses of 600 rat units three times daily for periods averaging three months. Five of the 6 were unrelieved.

The results as a whole were disappointing.

GROVER LIESE.

Moffat, William: Treatment of Menstrual Migraine, J. A. M. A. **108:** 612, 1937.

The result of treatment with gonadotropic urine extract in 17 cases of menstrual migraine, followed over a period of three years, was relief in all. Some, usually those who had suffered most severely over the longer periods of time, have been unable to discontinue treatment entirely.

In all but 4 of 11 cases studied, the sella turcica was found to be abnormal.

The following routine was evolved: Beginning with the fifth or seventh day after the onset of the menstrual flow a small dose, usually ranging from 2 to 6 rat units, is given; the dose is slightly increased daily until the tenth day, then rapidly increased, reaching a maximum of from 50 to 125 rat units on the fourteenth day, after which from 25 to 50 units are given daily until the onset of the next menstrual period.

The results tend to confirm the hypothesis that a leading factor in the production of menstrual migraine is an ovarian hypofunction, perhaps associated with an anterior pituitary hyperfunction.

GROVER LIESE.

Pasztor, M.: Ovarian Bronchial Asthma, Monatschr. f. Geburtsh. u. Gynäk. **105:** 161, 1937.

It is the opinion of the author that bronchial asthma can be connected with the female genital organs in a causal relationship. The attacks of bronchial asthma which occur during pregnancy and at the time of the menses are most likely due to the vagotonic effect produced by the estrogenic hormones. The attacks of asthma which occur during the menopause are due to a hormonic disturbance the primary cause of which is absence of ovarian function. For the attacks which occur during the menses, corpus luteum preparations should be given to diminish the excessive activity of the estrogenic hormones. During the menopause on the other hand, ovarian extract should be administered.

J. P. GREENHILL

Schäfer, W.: The Influence of Estrogenic Hormone on the Reactions of Allergic Organisms, Med. Klin. **33:** 1061, 1937.

Wiehler had observed that asthmatic women had an increase in their difficulties just before each menstrual period. Schäfer tried to determine the effect of ovarian preparations on the reactivity of sensitized female guinea pigs. He found that a much larger proportion of sensitized animals went into shock and died than not sensitized control animals. Hence an increased estrogen content in the body augmented the tendency to anaphylaxis in female animals. Schäfer warns physicians to give estrogenic substance to allergic patients only with great caution.

J. P. GREENHILL

Potter, Mabel F.: Oral Administration of Oestrin to Premature Babies, Brit. M. J. **1:** 1201, 1937.

The author reports the use of progynon in 11 premature babies and 1 sick baby with satisfactory results. Given orally, this form of estrin appears definitely

helpful in premature infants. The babies cause less anxiety; the feedings are taken better; the initial loss of weight appears less and is usually made up sooner. No baby to whom it was given died.

The arguments in favor of this therapy, according to Martin (1929), are (1) that the blood of newly born babies at term contains a comparatively large amount of estrin; (2) this is rapidly excreted by the kidneys in the first three or four days of postnatal life; (3) a baby born prematurely is at a disadvantage because it lacks the stimulus of the estrin which would normally have been present in its blood had it remained in utero; (4) the administration of estrin helps to make up this deficiency.

F. L. ADAIR AND S. A. PEARL

Romaniello, Giovanni: The Action of the Hormones Contained in the Urine of Pregnant Women Upon the Mammary Glands of Animals, Folia Gynaec. **33:** 2, 1936.

The author studied the action of the hormones in the urine of pregnant women upon anatomic development and function of the mammary glands of animals.

He found that the hormones affected the adult guinea pig mammary gland in such a manner as does pregnancy. In those already pregnant there occurred a relative hypertrophy; in those of puberty the glands approached the adult stage, as also did the mammary glands of castrated guinea pigs already in the stage of extreme atrophy.

MARIO A. CASTALLO

Engelhart, Erich: A New Action of the Lactation Hormone of the Pituitary and Its Effect on Ovary and Uterus, Klin. Wchnschr. **15:** 425, 1936.

It is well established that the lactation hormone of the pituitary will, when injected into female guinea pigs, produce a definite activation of the breasts and actual milk secretion. Engelhart followed this reaction for eight days and then killed the animals in order to study the effect of this hormone on the ovary and the uterus.

He was unable to find any ruptured follicles or corpora lutea in the ovaries. There was in each instance a well-developed luteinization of the ovaries which was demonstrable grossly as well as microscopically. On serial sections of the ovaries, degenerated follicles were found but no corpora lutea, and the diffuse luteinization was found throughout the entire ovarian stroma.

The uterine mucosa showed a typical pregravid reaction and the myometrium failed to contract in response to pituitary extract in the normal manner. The author believes therefore, that it may be possible to explain the puerperal amenorrhea and sterility of lactation by these actions of the lactation hormone on the ovary and uterus.

RALPH A. REIS

Dott, Ugo Mugnai: Prehypophysis and Lacteal Secretion, Riv. ital. di ginec. **19:** 505, 1936.

From a review of the literature relative to the production of mammary secretion and his own work the author draws the following conclusions: The hypophyseal gland, when stimulated by one hormone or another, responds with an increase of its own activity. The mammary glands respond to hypophyseal stimulation when they have been previously prepared by the ovarian hormones; however, they do not react in animals before puberty.

It would be very interesting, he states, to observe the lacteal secretion in adult hypophysectomized animals, treated with various other hormones.

AUGUST F. DARO

Mayor, José M.: The Inhibitory Effect of Follicular Hormone on Milk Secretion During the Puerperium, Zentralbl. f. Gynäk. 60: 2379, 1936.

Mayor summarizes the results of his observations by stating that the intramuscular injection of follicular hormone immediately following expulsion of the placenta exerts an inhibitory effect on the mammary glands of the puerperal woman.

Daily doses of 200 to 10,000 mouse units of follicular hormone, given over a period of six to eight days consecutively, do not show a clinically determinable inhibitory effect, whereas 250,000 mouse units of follicular hormone given in one dose produce a distinct inhibitory effect on the activity of the mammary gland.

Concerning the clinical application of these findings the author states that this form of therapy is being employed at his clinic in cases of stillbirths and abortions.

RICHARD E. SOMMA

Adrian, J.: Therapeutic Value of Injections of Folliculin in Cases of Undesired Secretion of Milk, Bull. Soc. d'obst. et de gynéc. 27: 331, 1938.

Research has demonstrated that estrogenic substances have a depressing action on the hypophysis and that the secretion of milk which depends upon the anterior pituitary hormone, prolactin, undergoes the same inhibition. He treated 100 women in whom it was desired to suppress the flow of milk by giving them a total of 60,000 units of estrin. This therapy brought about a reduction in the flow of milk only in 43 per cent of the cases. The preventive action of estrin was not encouraging.

J. P. GREENHILL

Ross, John R.: Prolactin—Its Effect on the Secretion of Woman's Milk, Endocrinology 22: 434, 1938.

Prolactin was administered, intramuscularly to mothers whose daily breast milk secretion on the fifth and sixth days was less than 400 c.c. The injections were given twice daily over a two-day period. One group of patients received a total of 400 U., whereas the second group received a total of 1,000 U. A control group of patients received intramuscular injections of normal saline.

The higher concentration of prolactin administered appeared to increase slightly the secretion of breast milk during the remainder of the stay in hospital. Of much more significance, however, was the fact that 7 out of 11 patients receiving this higher concentration of prolactin, whose records could be followed after discharge from the hospital, nursed their infants completely, whereas out of 8 such observed patients receiving the lower concentration of prolactin only 2 were able to nurse their infants completely. Of the 8 controls observed who received normal saline, only 1 nursed her infant completely.

Rather severe local reactions followed the injection of the larger amount of prolactin. It is probable that further purification of prolactin will eliminate these reactions. The administration of prolactin apparently has no effect on the fat, protein or ash content of the breast milk secreted. The effect obtained justifies further investigation. The urinary excretion of estrin in these cases was within the range found during the normal menstrual cycle.

J. THORNWELL WITHERSPOON

Dingemanse, Borchardt, and Laqueur: Male Hormones in Urine of Men and Women of Different Ages, Schweiz. med. Wchnschr. 67: 670, 1937.

They studied the amount of male hormone in the urine of men and women of different age groups. The male, like the female, hormones are eliminated in the urine in two different forms. The methods of determination formerly employed disclosed only the free form of the male hormone. However, a large

portion of the hormone is eliminated in the combined form. Thus the formerly detected quantities of 4 to 6 units of male hormone per liter of urine are much too low. By heating with acid, the hormone can be freed from the combination and thus becomes demonstrable. The authors summarize their observations: (1) The urine of healthy, sexually mature men contains 40 to 50 units. (2) The urine of healthy women contains approximately the same quantity of male hormone as does that of men (average, 30 to 60 units). (3) After sexual function has ceased, even during advanced senility and after castration, the urine still contains male sex hormone, but the quantities of the hormones are considerably less than in younger persons. (4) Boys and girls eliminate male hormone, but the quantities are smaller. (5) Pregnancy urine also contains male hormone. (6) It is improbable that the eliminated hormone originates in the ingested food.

J. P. GREENHILL

Korenchevsky: The Bisexual Properties and Co-operative Activity of Sexual Hormones and Their Effects on Females, Brit. M. J. 2: 896, 1937.

Bisexual properties have been found in nearly all the sexual hormones, and the cooperative activity of most of them with estrone and estradiol has been demonstrated on female rats experimentally. Suggestions are advanced as to the significance of these facts in regard to sexual physiology and pathology, and in relation to the therapy of general sexual disturbances in females. In the present state of knowledge, the author believes that the results of his experiments and those of other workers do not in any circumstances justify the use of the bisexual hormones with pronounced male activity in the treatment of diseases of women.

F. L. ADAIR AND S. A. PEARL

Groher, Hans: The Effect of Male Sex Hormone on Infantile Ovaries, Arch. f. Gynäk. **165:** 347, 1938.

The authors found that male sex hormones will stop the development of normal follicles in the ovaries of immature females almost completely. These follicles developing before the administration of male sex hormones underwent degeneration and became atretic. In addition to this atresia of primary follicles there also resulted a marked inhibition of development of the secondary follicles.

RALPH A. REIS

Mocquot, P., and Moricard, R.: Action of the Male Hormone (Acetate of Testosterone) on Castration Symptoms of the Female, Bull. Soc. d'obst. et de gynéc. **25:** 787, 1936.

The authors found that the administration of the acetate of testosterone modified and in general ameliorated the neurovegetative functional disorders which occur after castration in women. This substance, however, had no effect on the trophic vaginal disturbances secondary to castration. There may be a modification of the psychic state and in particular a sensation of euphoria and of increased activity but this effect is not constant. On the other hand there may result an increase in nervous instability.

J. P. GREENHILL

Zuckerman, S.: Inhibition of Menstruation and Ovulation by Means of Testosterone Propionate, Lancet 2: 676, 1937.

At this time it appears that any of the sex hormones will stop the estrous cycle. Estrin inhibits menstruation in monkeys and women, and so will progestin. This study is concerned with testosterone. One monkey which had had a reasonably regular menstrual cycle for 7 periods had a complete interruption of the cycle for 210 days when 25 mg. of testosterone were given twice weekly. A second monkey

had an amenorrhea of 122 days by the same treatment. Menstruation occurred eight days after discontinuation of the therapy. Detailed reports are given on the microscopic appearance of the ovaries.

Thus ovulation is suppressed in the normal mature monkey by estrin, and this study would indicate that temporary sterility could be secured and controlled by propionate testosterone. The masculinizing effects are slight and controllable. No changes occurred in the voice or hair growth, but the clitoris increased slightly. The internal reproductive organs remained uninjured, and menstruation was soon re-established with interruption of the therapy.

It is suggested that testosterone is worthy of clinical investigation to produce temporary sterility and to control uterine bleeding.

H. CLOSE HESSELTINE

Hartman, Carl G.: Menstruation Inhibiting Action of Testosterone, Proc. Soc. Exper. Biol. & Med. **37:** 87, 1937.

Testosterone and testosterone propionate inhibit the onset of menstruation in the normally cyclic monkey, after castration and after cessation of estrin injections.

In this sense this androgen simulates the action of progestin, as it does also in its stimulation of mammary development and in its inhibiting action on the vaginal mucosa. In its effect on the sex skin, however, it seems able to replace the estrogens, for this remained brilliantly red in a castrate for sixty-three days after estrin deprivation.

HUGO EHRENFEST

Foss, George L.: Action of Testosterone Propionate on the Female, Lancet **1:** 992, 1938.

In the opinion of the author metrorrhagia and menorrhagia can be controlled by the injection of testosterone propionate in adequate doses. In 16 cases a total dose of 300 to 800 mg. was required. In some of these, doses of 20 to 40 mg. given twice weekly for a few months were adequate, while in severe cases, dosages of 100 mg. daily or 150 to 200 mg. twice weekly were given. One patient failed to respond after a total dose of 2,800 mg.

A temporary therapeutic menopause with hot flushes may be induced with large doses so that menstruation is postponed for several months. Ovulation and luteinization are inhibited. The endometrium is in the resting stage. The breasts become smaller. There is definite increase in the size of the clitoris in some cases.

Before testosterone propionate can be regarded as a valuable addition to gynecologic practice its effects in large dosage over a long period of time must be studied.

CARL P. HUBER

Douay, E.: Some Uses of Testosterone Propionate in Gynecology, Compt. rend. Soc. franc. de Gynec. **8:** 165, 1938.

Douay used testosterone propionate in women. The first successful results in women were obtained in cases of premenstrual congestion and pain of the breasts. Testosterone produces a rapid diminution in the congestion of the breasts after administration of 5 mg. every two days beginning ten to twelve days before onset of the menses.

The author points out that testosterone is an antagonist to estrin. After three or four injections are given not only do the breasts diminish in size but the other signs of hyperestrinism disappear. Thus the abdomen becomes softer and smaller and the cervical discharge diminishes. The menses often occur on time or perhaps even somewhat early.

Injections are necessary still during the second month and the third month but only one injection may be necessary to produce the desired result.

In cases of menopausal disturbances the author advocates the combined use of estrin and testosterone.

J. P. GREENHILL

Novak, J., and Wallis, O.: Masculinization Followed by Re-Femininization, Arch. f. Gynäk. **164:** 543, 1937.

The authors describe the appearance of very marked and definite masculinizing symptoms and findings together with amenorrhea in a 32-year-old patient which were the result of a masculinizing tumor of the right ovary. This tumor was the size of a fist and grossly resembled a large corpus luteum on cross section. Microscopically the tumor is a typical luteoma rather than a tumor arising from misplaced suprarenal cortical cells because of the large lipoid contents of the individual cells. Removal of the tumor was followed by re-establishment of a normal menstrual cycle, a raise in the voice pitch, return of feminine contour and loss of most of the hirsutism which had developed. A résumé of the literature is included.

RALPH A. REIS

Glaser, E., and Haempel, O.: Hormonal Studies in a Case of Masculinizing Tumor of the Ovary, Klin. Wchnschr. **16:** 859, 1937.

The authors report their findings in a case of a 27-year-old woman with a masculinizing tumor of the ovary. The tumor had been present for approximately nine months and had produced typical masculinizing symptoms. The tumor was removed and no metastases were found. It proved to be a partially degenerated fibroma of the ovary, with only certain characteristics of the typical arrhenoblastoma. These findings were confirmed by the presence of relative large amounts of the female sex hormone in the blood serum. At the same time, large quantities of the masculinizing hormone were found in the blood stream, even though the tumor itself yielded comparatively small quantities. In contrast to this latter, much larger quantities of the masculinizing hormone were found in the cyst fluid from a cyst of the opposite ovary. The authors recommend the early estimation of the hormone content of the blood serum in all suspected cases of masculinizing tumors.

RALPH A. REIS

Lepper, E. H., Pratt, C. L. G., Pratt, F. B., and Vaux, D. M.: Hormone Content of Ovarian Tumours, Lancet **1:** 249, 1938.

The concentration of estrin was determined in 8 follicular cysts associated with typical hyperplasia of the endometrium. It was found to be present in approximately the same degree as in the ripe follicle but due to the larger amounts of fluid present the absolute amount of estrin in the ovary was considerably increased.

A total of 70 ovarian tumors and pre-operation urine specimens were examined for prolan A and B and for estrin. Prolan A was found in larger amounts in cyst fluid and urine in malignant tumors than in benign ones but was found in all types of the benign group. Prolan B was found in the cyst fluid of 2 out of 3 pregnant patients. Estrin was found in all follicular cysts. It was also present in the fluid from 2 of 11 germinal cysts but in very low concentration.

CARL P. HUBER

Kriss, B.: Feminizing Action of Male Sex Hormones, Monatschr. f. Geburtsh. u. Gynäk. **106:** 157, 1937.

The author found that a lipoid male sex hormone derived from bull's testicles produced typical estrus changes in the vaginas of castrated female white mice. The same type of estrus changes were also produced by using a watery solution of androsterone. The author treated 48 women who had hypohormonal amenorrhea by means of male sex hormone and he observed good results in 50 per cent of the cases. The menses returned and continued after cessation of the treatment.

J. P. GREENHILL

Fels, Erich: Progesteron and the Male Genital Tract, Arch. f. Gynäk. **160:** 461, 1936.

Fels carried out a series of animal experiments to determine the effect of progesterone on the male genital tract of animals. It is well known that estrin has a definite effect on the male genital tract. He was unable to find any changes ascribable to the progesterone either in an antagonistic or in a synergistic way. Such changes can only be produced by estrin.

RALPH A. REIS

Friedlander, E., and Moses, E.: Secondary Pregnancy Reactions in Chorio-Epithelioma of the Male, Wien. klin. Wchnschr. **22:** 684, 1936.

The occurrence of chorioepithelioma in men has been reported in about 130 cases. Heidrich, Fels and Mathias found the anterior pituitary hormone in the urine in larger quantities with this tumor than in pregnancy. B. Zondek also found A. P. R. I-III reactions in three cases of malignant tumors of the testicle. In one case, hydrocele fluid also gave a positive reaction. These authors report a case of chorioepithelioma in a man 36 years of age. The symptoms were hemoptysis, loss of weight, and enlargement of the breasts. There were metastases to the lungs and retroperitoneal lymph glands. The patient died and the gross and histologic findings were verified. The testicular tumor contained in addition to a chorioepithelioma a seminoma, an epithelioma, and an epidermoid cyst. The hormonal influences of this tumor produced a gynecomasty with similar pregnancy changes and typical pregnancy changes in the hypophysis.

W. B. SERBIN

Item

American Board of Obstetrics and Gynecology

The general oral, clinical and pathological examinations for all candidates, Part II Examinations (Groups A and B), will be conducted by the entire Board, meeting in St. Louis, Missouri, on May 15 and 16, 1939, immediately prior to the annual meeting of the American Medical Association. Notice of time and place of these examinations will be forwarded to all candidates well in advance of the examination dates.

Candidates for reexamination in Part II must request such reexamination by writing the Secretary's Office before April 1, 1939. Candidates who are required to take reexaminations must do so before the expiration of three years from the date of their first examination.

Application for admission to Group A, May, 1939, examinations must be on file in the Secretary's Office by March 15, 1939.

Application blanks and booklets of information may be obtained from Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

Books Received

THE QUEEN CHARLOTTE'S TEXT-BOOK OF OBSTETRICS. By Members of the Clinical Staff of the Hospital. Fifth edition, with 4 colored plates and 293 text figures, 668 pages. J. & A. Churchill Ltd. London, 1938.

FUNDAMENTALS OF DENTISTRY IN MEDICINE AND PUBLIC HEALTH. By John Oppie McCall, Director of the Murry and Leonie Guggenheim Dental Clinic, New York, etc. 50 illustrations, 161 pages. The Macmillan Co., Inc., New York, 1938.

THE FUNDAMENTALS OF INTERNAL MEDICINE. By Wallace Mason Yater, Professor of Medicine and Director of the Department of Medicine, Georgetown University School of Medicine, etc. First edition, with 255 illustrations, 1021 pages. The Macmillan Company, Inc., New York, 1938.

CLINICAL LABORATORY METHODS AND DIAGNOSIS. A textbook of laboratory procedures with their interpretation. By R. B. H. Gradwohl, M.D., Director of the Gradwohl Laboratories, etc. Second edition, with 492 illustrations in the text and 44 color plates, 1607 pages. The C. V. Mosby Company, St. Louis, 1938.

THE PRACTICE OF MEDICINE. By Jonathan Campbell Meakins, M.D., Professor of Medicine and Director of the Department of Medicine, McGill University, etc. Second edition, with 521 illustrations including 43 in color. The C. V. Mosby Company, St. Louis, 1938.

CONTROL OF CONCEPTION. By Robert Latou Dickinson, M.D., Former Clinical Professor of Obstetrics and Gynecology, Long Island College Hospital, etc. A clinical medical manual with numerous original illustrations by the author. Second edition, 390 pages. Williams & Wilkins Company, Baltimore, 1938.

GEBURTSHILFLICHE UND GYNAEKOLOGISCHE THERAPIE, mit Einschluss der Heilmittel. Von Dr. Georg Burckhard, o. Professor der Geburtshilfe und Gynaekologie, Universitaet Wuerzburg. Zweite, umgearbeitete Auflage, 260 Seiten. Verlag von Ferdinand Enke, Stuttgart, 1938.

HANDBOOK ON CANCER, for the medical profession. The Authorship Committee, Department of Cancer Control, Canadian Medical Association, Toronto, 1938.